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PITYRIASIS LICHENOIDES AND PARAPSORIASIS.

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It is just fifty years since Brocq with sure clinical instinct grouped together under the name of parapsoriasis a variety of eruptions which he suggested had some affinity with psoriasis, seborrhoeides and lichen planus. Though the name parapsoriasis which he chose was in some ways unfortunate no better has been suggested, and time has confirmed much of Brocq's conception of the close relationship of most of these affections. He emphasized the minimal infiltration, the slow evolution, the absence of itching, the lack of response to treatment and the little tendency to healing.

A review of the position to-day would seem to justify some reorientation of the problem, and the recognition of the significance of certain manifestations and relationships which are probably acceptable to the majority of dermatologists. Pityriasis lichenoides and parapsoriasis, though not common diseases, are not rare, and most would agree that pityriasis lichenoides should not be regarded as a form of parapsoriasis.

PITYRIASIS LICHENOIDES.

Pityriasis lichenoides chronica, described by Juliusberg in 1899, and its variant pityriasis lichenoides et varioliformis acuta, named by Habermann in 1925 and originally described by Mucha in 1916, should be regarded as a single entity, should be accepted as distinct from parapsoriasis guttata, and should be removed entirely from the group of parapsoriasis. It is an affection seen most commonly in the young, it retains its particular characters throughout its course and would appear to be a self-limited disease lasting from a few months to several years. The affection never passes into any of the other types of parapsoriasis and never gives rise to a malignant reticulosis.

The individual lesions in this eruption are approximately $\frac{1}{2}$ cm. in diameter, start as macules, pass through the stage of lichenoid papule with mica scale

and resolve in the course of three or four weeks ; this time is variable, and may be as short as two weeks or as long as six weeks. Sometimes purpura, vesication and necrosis occur and leave varioliform scarring. This course of evolution is quite regularly maintained throughout the duration of the affection from its onset. The diagnosis has been made confidently with an eruption of two weeks' duration, still under observation five years later and still of the same pattern though rather less profuse. Sometimes there appears to be direct response to treatment by such measures as gold injections, ultra-violet light therapy, calciferol and thorium X, but this is not at all constant.

Thirty-two patients with pityriasis lichenoides have been studied. The distribution on trunk and limbs particularly recalls pityriasis rosea. In two patients lesions were seen on the penis, in one on the mucosa and in one on the palms ; in two on the face, and in one patient on tongue and lip, but these were unusual sites. The appearances may suggest at first glance a diagnosis of syphilis, psoriasis, chicken-pox, urticaria pigmentosa, lichen planus, scabies, or pityriasis rosea. These can, however, usually be dismissed after careful study. Occasionally an illness appeared to provoke an attack—a fracture in two cases, a surgical operation in two cases, influenza, an examination, worry and bursitis in others.

The histology of the papule is not diagnostic and varies with the stage of evolution. At its height there is marked oedema of the papillary layer of the dermis and of the epidermis with some hyperkeratosis. There is a striking infiltration in the upper part of the dermis and passing into the epidermis, consisting essentially of small round cells, fibroblasts and occasional histiocytes, and a broad cuffing of the vessels throughout the dermis with a similar infiltrate. These features, while not diagnostic, are marked, and are very much greater than those observed in parapsoriasis en plaques or in the guttate form of that disease. Civatte (1951) has drawn attention to the histological differences between these papules and those seen in parapsoriasis.

In a series of 20,000 patients seen in private practice in the past twenty-five years pityriasis lichenoides has been diagnosed in 10 patients and parapsoriasis of one form or another in 26. The earliest age of onset in pityriasis lichenoides chronica was four years and the average age of onset twenty-three years, whereas in parapsoriasis the average age of onset was forty years. In the last 70,000 patients recorded in the out-patients' department of the General Infirmary at Leeds pityriasis lichenoides was diagnosed in 31 patients and parapsoriasis in 45.

It has been possible to follow 32 of these patients with pityriasis lichenoides for a number of years ; 13 were females and 19 males, and 16 showed acute lesions at times. Twenty patients are known to have recovered and to have been clear now for periods varying up to seventeen years. In this group the disease lasted from three, six, nine, twelve, eighteen months and three years

up to seven years—the last patient being observed throughout the course of the disease and having now been clear for two years.

In another patient who has now been clear for five years, the eruption became gradually less profuse over a period of four years before it disappeared. One patient who has now been under observation for five years improved markedly after removal of one ovary three years ago but still presents a few typical papules at each examination. In yet another the eruption which had been present for two and a half years cleared during pregnancy, but gradually relapsed three months after confinement and is now again profuse. The affection was not altered in one patient by an attack of measles.

Of the patients who have not cleared seven are still under observation and two of these have been affected for five years and two for three years. Some of these patients, although apparently clear, state that they get an occasional papule but it has not been possible to confirm this. One patient in her twenties, presenting a typical eruption in every other respect, would develop small verrucose lesions resembling seborrhoeic warts on the back, in the site of some papules. These subsequently cleared.

Three patients have left the region. One, affected for fourteen months before she left for Malta, appeared to be clearing; each papule in this patient persisted about one month. In a second patient the eruption had started two months after an operation on her gall bladder. In a third, affected for three years, the papules coming in showers, the eruption had started two years after returning from India, where she had resided for twenty-five years. The patient was sensitive to sunlight but her pityriasis lichenoides was worse in winter. Two patients cannot now be traced.

The importance of separating the disease pityriasis lichenoides chronica and pityriasis lichenoides et varioliformis acuta from parapsoriasis in general lies in the fact that the ultimate prognosis is good, that malignant forms of reticulosis will not supervene and that recovery is to be expected.

Confusion may arise in the early stages because of the presence of similar lichenoid papules with any of the patterns of parapsoriatic eruption.

PARAPSORIASIS PROPER.

In parapsoriasis proper we have a clinical entity in which the elementary lesion is a fawn, scaling erythema relatively fixed and persistent. A site once involved is always affected, though the lesions may wax and wane, fade and recur, sometimes seasonally. Lesions may enlarge and alter in outline but appear to be persistent through life.

Different patterns are seen and may sometimes change with time in the same patient; mixed patterns are commonly observed. The lesions may be guttate, of finger-print, bizarre, discoid or sheet outline, or may be interlacing and reticular. Although commonly macular and finely scaling, lesions may be

substantial and psoriasiform, without there being any significant histological infiltration.

The main patterns described by Brocq are still recognized and form the basis of our clinical descriptions, though it would seem that intermediate forms are common. The guttate form of parapsoriasis, which is probably no more than a guttate form of parapsoriasis en plaques, is not unlike pityriasis lichenoides, but the lichenoid and mica-scaling features are not distinctive as in the latter disease and the life-history of the individual papules is different. In parapsoriasis guttata the papules, though they may wax and wane, persist. Generally the papules are little more than macular, but sometimes they are quite psoriatic in appearance. They do not, however, come and go with the regular rhythmical periodicity seen in pityriasis lichenoides chronica. Nevertheless, the differentiation may be difficult without prolonged observation.

Parapsoriasis en plaques presents as macular, fawn, scaling lesions of variable size and outline, often suggesting an artefact, frequently symmetrical, especially on arms and thighs (Fig. 1). Lesions may sometimes assume a large plaque or sheet pattern, as in the xanthoerythroderma perstans of Radcliffe-Crocker. The lesions of parapsoriasis en plaques, again, are usually macular, but they may be substantial in a psoriatic form. Histological appearances are trivial and insignificant—a slight, round-celled perivascular infiltration and parakeratosis.

The third pattern is parapsoriasis lichenoides, so named by Brocq because of its approach to eruptions of the lichen planus type. It was considered in detail by Unna, who used the term parakeratosis variegata. This affection is seemingly an infiltrated eruption of papules and streaks, assuming a coarse, retiform pattern on flanks and abdomen, thighs and forearms particularly, and having a purplish tint with slight scaling. There is usually much pigmentation and the scalp and face may be involved—indeed any part of the integument. Histologically, there is a non-specific round-celled infiltration in the corium, but this is not as considerable as clinical appearances would suggest. Lymph-node enlargement is not significant.

In a series of 26 patients with various types of parapsoriasis proper 11 were females and 15 males. The earliest onset was at the age of ten years, the average age of onset was about forty years.

Any of those patterns of parapsoriasis may persist for twenty years or more before any more serious change occurs, though such changes may be present from an early stage. They turn upon a reticular patterning, fine or coarse, with pigmentation, ectasia of the vessels and sometimes atrophy. Such patterning is clearly determined by vascular influences. Dermatologists in many countries have drawn attention to these features and their relevance to subsequent neoplastic changes of a reticulosis character. Leukaemia, Hodgkin's disease, mycosis fungoides and lymphoblastomata have all been described in this connection. Some have gone so far as to say that this is the

inevitable course of a case of parapsoriasis proper. It is, at all events, a fact that such changes may supervene in any type or pattern of parapsoriasis proper (but not in pityriasis lichenoides), that changes from one pattern to another occur in the same patient, and that intermediate patterns are often seen. Brocq noted this in his original observations.



FIG. 1.—Parapsoriasis en plaques showing bizarre character.

Two points need emphasis here, both of which have been given attention by various writers. The first is the fact that identical reticular patterning of the eruption is seen in poikiloderma atrophicum vasculare with telangiectasia, atrophy and a tendency to neoplastic change. The second point is that papular lesions, not unlike those of pityriasis lichenoides, may be seen as has been mentioned, with all these patterns of parapsoriasis proper and also with poikiloderma atrophicum vasculare. They may go on to more intense cellular infiltration and later to necrosis. They may gradually attain a larger size

than the lichenoid papules of pityriasis lichenoides, and they may be the precursor of the phase of malignant reticulosis.

It would seem certain that any of the more simple patterns of parapsoriasis proper—those devoid of reticular patterning, telangiectasia, atrophy or infiltrated papules—may run their course to the end of the patient's life without undergoing grave or malignant change. That does not exclude the possibility that with a longer life such change might have arisen. Nor does it state, since I do not know, whether any such cases recover, but I suspect that they do. MacCormac reported such happening.

In discussing parapsoriasis proper mention should be made of the related cases described by Whitfield under the term dermatitis colonica, where parapsoriasiform appearances were associated with and seemingly dependent upon the balance of the flora in the bowel and were reversible at will. I believe I have seen such cases. The point is important in relation to aetiology.

Pityriasis lichenoides chronica, with its acute phase, may well be a disease *sui generis* with a specific cause and for which there may be found a specific cure, but in my submission the clinical entities we gather under the title of parapsoriasis proper are clearly symptom complexes and not pathological entities. That line of approach is fashionable, but is profitable and likely to favour some advance in our knowledge, as we have seen in its application to such syndromes as dermatomyositis, acute lupus erythematosus and pemphigus. We may probably assume that both parapsoriasis proper and poikiloderma atrophicans vasculare are primarily reactions of the reticulo-endothelial tissues bearing gravely upon the vascular system.

Reticular Patterning.

In connection with the reticular patterns in parapsoriasis attention may be drawn to similar features of reticular telangiectatic purpura of fine pattern seen in the leukaemias and allied disorders and with drugs and chemicals which damage the smaller vessels, such as carbromal (Adalin), and with textile dressings. Similar though often coarser patterns are seen with such changes as accompany vascular insufficiency in the lower limbs, especially where there is damage to the smaller arterioles and capillaries. It is occasionally seen with syphilitic damage to vessels and in tuberculosis, arteriosclerosis, and such allergic disorders as polyarteritis nodosa. It is perhaps relevant to note the resemblance between some drug eruptions and parakeratosis variegata. With mepacrine and with such metals as gold, bismuth and arsenic, lichenoid and reticular eruptions which may or may not be preceded by pityriasiform erythematous lesions and may or may not be followed by atrophic changes are sometimes indistinguishable from parapsoriasis lichenoides (parakeratosis variegata). I have seen parapsoriasis heralded by a sparse, patchy eruption

in partial livedo pattern—I have seen disseminate lupus erythematosus and sarcoidosis fade through the same pattern.

DISCUSSION.

In considering the aetiology of parapsoriasis as a group there are two possibilities suggested by these observations. Is parapsoriasis to be regarded as the expression of a reticulo-endothelial disease, benign in most of its manifestations, but capable of malignant change? Some have suggested that all cases are potentially malignant, the parapsoriasiform stage corresponding to the premycotic stages of mycosis fungoides.

Alternatively, is parapsoriasis a fixed toxic eruption comparable with certain chemical and drug eruptions or some eruptions emanating from metabolites consequent, for instance, on disturbed bowel function, the damage bearing mainly upon the smaller vessels and ultimately giving rise to changes not dissimilar from those following radiation therapy? In this case malignant changes would be presumed to be a secondary phenomenon consequent upon the vascular and local nutritional damage and again comparable with the malignant changes which supervene on radio-atrophy. This latter conception might more easily explain the strange resistance of parapsoriasiform eruptions to x-ray or radium therapy and the response—if only temporary—to thorium X. I am aware that the analogy with radiotherapeutic atrophy is not an exact one and that the malignant change here is usually epidermal, but I suspect that an underlying pathology may be common to both conditions.

The second hypothesis would seem to be the more likely, that parapsoriasis proper is a symptom complex rather than a disease *sui generis*. It would follow from such an hypothesis that we should investigate more fully these cases with a view to discovering an exogenous or endogenous agent acting as the exciting vascular irritant, and it may be that a study of analogous vascular disorders would throw further light on aetiology and treatment of this serious affection.

SUMMARY.

1. It is suggested that pityriasis lichenoides is a self-limited disease which resolves spontaneously and does not give rise to serious sequelae.
2. Pityriasis lichenoides should not be included in the group of parapsoriasis.
3. Parapsoriasis proper may proceed to one of the many types of malignant reticuloses and be fatal.
4. Certain analogous skin changes are considered in relation to the aetiology of parapsoriasis.

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SKIN DISEASE IN THE BRITISH ARMY IN S.E. ASIA.
 II: *TINEA CORPORIS*: CLINICAL AND PATHOLOGICAL
 ASPECTS, WITH PARTICULAR REFERENCE TO THE
 RELATIONSHIP BETWEEN *T. INTERDIGITALE* AND *T.*
MENTAGROPHYTES.

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In the preceding paper (Sanderson and Sloper, 1953*a*) the results of a survey of skin disease among British troops in Malaya and Hong Kong are described. Ringworm of the body was found in 33·5% of 1424 men examined on duty. This high incidence, and the florid nature of the cases, prompted us to make a detailed clinical and pathological investigation of the disease, an account of which is given in this paper.

PATHOLOGICAL METHODS.

In general, laboratory investigations consisted solely of an attempt to recover the organism in pure culture. The direct examination of skin scrapings for the presence of mycelia was not a routine procedure, although it was occasionally used.

Sites to be scraped were wiped with cotton wool soaked in 70% alcohol ; tissue was then removed with a Bard-Parker scalpel. In scraping toe clefts, care was taken to avoid heaped-up dead skin, and to seek vesicles. The scalpel blades were cleaned and flamed before and after scraping each site. The scrapings so obtained were placed in paper packets ; subsequently fragments were planted out on agar slopes, test-tubes being closed with waxed plugs. Primary cultures were made on three different media : beerwort agar, beerwort agar containing 0·04% sodium tellurite, and maltose peptone agar containing 0·001% gentian violet and 0·04% sodium tellurite. Alkaline maltose agar (Leise and James, 1945) was also frequently used. Subcultures were made on to maltose peptone agar. The tubes were kept at room temperature (about 27° C.). Growth on the media containing sodium tellurite was slow, and subcultures were made as soon as it seemed likely that pathogens were present. In the early stages of the investigation half the material from each

site was put in a separate paper packet and sent to Dr. J. T. Duncan for examination at the London School of Tropical Medicine and Hygiene. This procedure was followed for the first 200 of about 1400 scrapings, at which stage it had become clear that our results showed excellent agreement with Dr. Duncan's; the practice was then discontinued.

The terminology used in this paper is that recommended in the Memorandum on the Nomenclature of Fungi published by the Medical Research Council (1949). Particular interest attaches to two organisms: *Trichophyton mentagrophytes* (Robin) Blanchard, and *Trichophyton interdigitale* Priestley.

Both clinically and in culture these appear to be separate organisms. However, because of the tendency of *T. mentagrophytes* to produce, *in vitro*, variants closely resembling *T. interdigitale*, it has been suggested that the latter should be regarded as a degenerate form of *T. mentagrophytes* (Emmons, 1932; Epstein, 1938; Emmons and Hollaender, 1945). Many workers have, in fact, ceased to draw any distinction between the two organisms (Peck *et al.*, 1944; Ajello *et al.*, 1945; Hopkins *et al.*, 1947). There is, however, no convincing evidence that *T. mentagrophytes* has ever been derived from *T. interdigitale*. Weidman's (1926) clinical observations can only be regarded as speculative, while it is not apparent that the increased pathogenicity observed by Epstein in *T. interdigitale* was accompanied by any morphological change. In this paper the organisms are treated as separate and distinct, although the possibility that they are closely related, and may even undergo transformation the one into the other, is not excluded.

RESULTS.

A. Body Ringworm.*

(i) Clinical Features.

The high rate of body ringworm revealed by the survey has already been noted. Table I gives the results in greater detail. In Malaya throughout the year, and in Hong Kong during the summer, about a third of the European soldiers examined were affected. The incidence in different units varied between 11.3% and 57.2% in Malaya, and between 24.3% and 53.2% in Hong Kong. By contrast, among 150 locally enlisted Asiatic troops and 122 British service-women the rates were 6.7% and 9.8% respectively. The lesions included erythematous areas with a scaling edge in the skin folds, especially the crutch (Hebra's "eczema marginatum"); circinate scaling patches on the limbs or trunk, often vesicular or pustular at their edges, and with a tendency to central healing; and deep follicular, purulent lesions in areas of strong hair growth.

The disease often took a florid form; cases having 20-30 lesions when first seen were not uncommon, and no area of the skin seemed to be exempt.

The anatomical distribution of lesions or groups of lesions in 497 successive cases is shown in Table II.

* Body ringworm is defined here as ringworm on any site other than toe clefts, toe flexures, heels or soles. A lesion on the dorsum of foot, unless continuous with a cleft lesion, is counted as body ringworm.

TABLE I.—*The Incidence of Tinea corporis among Troops in the Far East.*

Population.	Where examined.	Number examined.	Number with body ringworm.	% with body ringworm.
European soldiers . . .	Hong Kong .	636 .	241 .	37·8
European soldiers . . .	Malaya .	788 .	237 .	30·1
Chinese, Malay and Indian soldiers	Malaya .	150 .	10 .	6·7
European service-women .	Malaya .	122 .	12 .	9·8

TABLE II.—*Anatomical Distribution of Lesions in 497 successive Cases of Tinea corporis and cruris.*

Site.	Number of cases showing involvement of this site.	% of cases showing involvement of this site.
Scalp or face	20 .	4
Shoulder	18 .	3·6
Axilla	24 .	4·8
Arm	16 .	3·2
Hand	5 .	1
Trunk, excluding belt area .	49 .	9·9
Belt area	87 .	17·8
Crutch	347 .	70
Buttock	99 .	20
Leg	68 .	13·9
Dorsum of foot	40 .	8

It will be seen that by far the commonest site of lesions was the crutch, which was involved in nearly three-quarters of the cases examined. In fact, in 165 of the 347 cases so affected, no other body lesions were found, and for this reason it seemed probable that in the remaining 182 cases the crutch was the first site to be affected.

A number of the cases showed a tendency to deep involvement of the hair follicles, leading to boggy, indurated and tender areas from which pus oozed. This was commonest in regions of strong hair growth, e.g., beard area, scalp, pubes, and sometimes legs and arms. Such cases appeared to be resistant to all anti-fungal therapy but healed spontaneously, usually with some scarring, in about six weeks.

(ii) *Laboratory Findings.*

Dermatophytes were recovered from body lesions in 114 Europeans and 9 Asiatics. Some of these cases were investigated because they exhibited unusual varieties of ringworm, and others because their lesions were particularly well suited for the trial of various therapeutic agents. To this extent the series was not a random one, although most of the cases investigated were not specially selected. The results are summarized in Tables III and IV.

It will be observed that from 114 cases, 126 positive cultures are recorded; this is because several of the subjects were infected, either simultaneously or

TABLE III.—*An Analysis of 126 Dermatophytes Isolated from Lesions of the Body in 114 Europeans and of 9 Isolated from 9 Asiatics.*

Number of cases.	Dermatophytes.	<i>T. mentagrophytes.</i>	<i>E. floccosum.</i>	<i>T. interdigitale.</i>	<i>T. rubrum.</i>	<i>T. violaceum.</i>
114 Europeans.	126	77 (61%)	42 (33·3%)	1 (0·8%)	5 (4%)	1 (0·8%)
9 Asiatics	9	1	1	0	7	0

successively, with more than one organism. This phenomenon of mixed infections will be discussed in greater detail later.

Table III shows clearly the dominant part played in infections of Europeans by *T. mentagrophytes* and *E. floccosum*: these two organisms accounted for all but 6% of the infections. In the few Asiatics examined, on the other hand, the predominant organism was *T. rubrum*.

TABLE IV.—*The Anatomical Distribution of 233 Sites of Infection by Known Organisms in 114 Cases of Tinea corporis.*

Site.	<i>T. mentagrophytes.</i>	<i>E. floccosum.</i>	<i>T. rubrum.</i>	<i>T. violaceum.</i>	<i>T. interdigitale.</i>	<i>E. floccosum</i> and <i>T. mentagrophytes.</i>
Scalp and face	15	—	1	—	—	—
Neck and shoulders	8	2	—	—	—	—
Axillae	2	1	1	—	—	—
Arms	8	—	—	—	—	—
Hands	5	—	—	—	—	—
Trunk, excluding belt	34	8	3	—	—	—
Belt region	13	9	2	—	—	1
Crutch	30	32	4	1	—	3
Buttocks	11	—	1	—	—	—
Legs	21	9	—	1	—	—
Dorsum of feet	8	2	—	—	1	1
	155	63	12	2	1	5

It will be seen that both *E. floccosum* and *T. mentagrophytes* were responsible for lesions on most parts of the body. Sporadic infection with *E. floccosum* usually tends to be confined to the flexures; however, involvement of trunk and limbs by *E. floccosum* is also well recognized (Mercer and Farber, 1935; Hopkins *et al.*, 1947). *T. mentagrophytes*, on the other hand, usually attacks non-flexural areas; its frequent occurrence as a cause of crutch infections in this series is therefore worthy of note. It was of particular interest that such trichophytic crutch infections were often clinically indistinguishable from those due to *E. floccosum*, a point previously emphasized by Fischer (1917) and by Pautrier and Rietman (1922). Indeed, the only reliable clinico-pathological correlation appeared to be in the deep suppurating variety of tinea mentioned above, for every lesion of this kind which was investigated yielded *T. mentagrophytes*.

B. *Ringworm of the Feet.*(i) *Clinical Features.*

Tinea corporis is easily recognized, and the diagnosis is readily confirmed by direct microscopy and by culture. *Tinea pedis*, on the other hand, presents a less definite picture, and demonstration of the causative organism is much more difficult and uncertain. For this reason no attempt was made in the clinical survey to diagnose fungus infection of the feet. Instead, all cases showing maceration, redness or scaling in the toe flexures or clefts, together with those showing vesicles or their remains in these sites, were grouped together, without prejudice as their possible aetiology, as "dermatoses of the feet." It is probable that in this examination of the feet of 1424 men many minimal lesions were overlooked.

In a succeeding paper (Sanderson and Sloper, 1953c), details are given of the correlations in these cases of clinical appearances with laboratory findings, and of the criteria for the clinical diagnosis of *tinea pedis* which were evolved on this basis. For the purposes of the present paper it will suffice to say that it seems unlikely that the overall rate of fungus infection of the feet could have been less than 50% ; it may in fact have been higher.

(ii) *Laboratory Findings.*

Pathogenic fungi were recovered from the feet of 85 men (all European). The species-distribution of these is shown in Table V.

TABLE V.—*An Analysis of 96 Dermatophytes Isolated from Lesions of the Feet in 85 Europeans.*

Number of cases.	Dermatophytes.	<i>T. mentagrophytes.</i>	<i>E. floccosum.</i>	<i>T. interdigitale.</i>	<i>T. rubrum.</i>
85	96	39	43	11	3
		(40·6%)	(44·8%)	(11·5%)	(3·1%)

It will be seen that *T. mentagrophytes* was recovered from the feet rather less commonly than *E. floccosum*, the reverse of the situation on the body (Table III). However, the predominance of these two organisms in both sites is clear ; on the body they accounted for 94% of the infections identified, and on the feet for 85%. Mixed infections by both organisms were encountered, but were only recognized by means of pathological investigations ; it proved impossible to distinguish clinically between infections due to *E. floccosum*, *T. mentagrophytes* and *T. interdigitale*.

It may be objected that any study of *tinea pedis* should include an account of nail infections. Such infections, however, are unlikely to have contributed greatly to the prevalence of body ringworm in this outbreak, since the dominant organisms (*E. floccosum* and *T. mentagrophytes*) rarely, if ever, affect the nails (Dr. J. T. Duncan, personal communication).

Mixed Infections.

It has already been noted, in connection with Tables III and V, that the number of infections recorded was greater than the number of cases, and that the discrepancy was due to the isolation of more than one organism from some cases. These mixed infections occurred in 26 (17·8%) of the 147 cases from which dermatophytes were recovered. In two of these, three different organisms were recovered from each patient: in the remaining 24 the infection was due to two different organisms.

Mixed infections of this kind should perhaps be expected in any outbreak of ringworm due to two or more fungi. Nevertheless, they deserve mention, since until comparatively recently they have been regarded as curiosities. Thus Muskatblit (1941), who described six instances, was only able to find another 36 recorded by previous workers. However, Lewis and Hopper (1943) described 23 more cases, and remarked that such infections were probably commoner than had been thought in the past. This was confirmed by Hopkins *et al.* (1947), who found them in 5·7% of 1700 cases of *tinea pedis*. The corresponding figure for *tinea pedis* in this series is 13% of 85 cases.

Because of the interest taken in such cases, it is worth while analysing them further. The following classification, due to Lewis and Hopper, is convenient:

- (1) Combined: two or more organisms recovered from a single site at the same time.
- (2) Concurrent: two or more organisms recovered simultaneously from different sites.
- (3) Consecutive: two or more organisms recovered at different times from the same case.

These categories are not mutually exclusive, and in the 26 instances of mixed infections in this series, there were 9 combined infections, 16 concurrent infections and 10 consecutive infections. In all the combined infections the organisms were *T. mentagrophytes* and *E. floccosum*. This was also the case with the concurrent and consecutive infections, except in six instances: in three of these the infections were by *T. interdigitale* and *E. floccosum*, and in the remaining three by *T. interdigitale* and *T. mentagrophytes*, by *T. interdigitale*, *T. mentagrophytes* and *E. floccosum*, and by *T. mentagrophytes*, *T. rubrum* and *E. floccosum* respectively.

DISCUSSION.

The proclivity to ringworm infections displayed by Europeans, and in particular by European soldiers when serving in the Far East, is well recognized. Little work has been done, however, on the clinical, pathological and epidemiological aspects of this problem. Our observations partly remedy this neglect and are of more than local significance, since they are concerned with Europeans infected by organisms encountered in Europe. Consequently,

the unusual features of the disease as seen in the Far East, for example its severity and the behaviour of *T. mentagrophytes*, merit close attention.

The Prevalence of Tinea corporis.

Figures not very different from those inferred for tinea pedis in this series have been recorded by several authors (Peck *et al.*, 1944; Ajello *et al.*, 1945; Hopkins *et al.*, 1947), and in view of the diagnostic difficulties mentioned above, a more detailed comparison is unlikely to be profitable. In the case of body ringworm, however, this diagnostic problem does not exist, and a direct comparison of this series with those of other workers is possible. Such a comparison has been made in Table VI.

TABLE VI.—*Previous Descriptions of Widespread Body Ringworm.*

Author.	Date.	Place.	Climate.	Incidence.	Organism.	Remarks.
Jacobi	1907	Germany	Temperate	Almost every individual undergoing treatment	Trichophytic	—
Sabouraud	1910	Paris	"	23 cases in over 1 year	<i>E. inguinale</i> (<i>E. floccosum</i>)	Boy's school.
Fischer	1917	Berlin	"	17 cases in over 1 year	<i>T. grandulosum</i> (<i>T. mentagrophytes</i>)	Hospital cases.
Gutmann	1919	Breslau	"	17 cases in 6 months	<i>T. grandulosum</i> (<i>T. mentagrophytes</i>)	Ditto.
Pautrier and Rietman	1922	Strasbourg	"	100 cases in at least 1 year—all manicured lunatics	<i>T. grandulosum</i> (<i>T. mentagrophytes</i>)	Cases confined together; undergoing hydrotherapy.
Mercer and Farber	1935	Atlantic liner	"	6% of 300 men at one examination	<i>E. floccosum</i>	Liner crew.
Hopkins <i>et al.</i>	1947	North Carolina	Cold in winter and humid in summer	357 cases in over 4 years	<i>T. purpureum</i> (<i>T. rubrum</i>) <i>E. inguinale</i> (<i>E. floccosum</i>) rarely <i>T. gypsum</i> (<i>T. mentagrophytes</i>)	White and negro soldiers in scattered units.
Fergusson	1948	Thailand	Hot and humid	55% of unit of unspecified size	—	Prisoners of war: the disease described as "ringworm."
Jolly	1948	Java	Ditto	22.5% of 400 men	—	Soldiers doing heavy manual labour.
This series	—	Malaya; Hong Kong	"	33.5% of 1424 men	<i>T. mentagrophytes</i> and <i>E. floccosum</i> ; occasionally <i>T. rubrum</i>	British soldiers.

It will be appreciated from this table that the incidence of body ringworm in our series was extremely high. Indeed, we have been unable to find a description of any group worse affected than one we investigated in Malaya, in which 57% of 74 men were affected.

The Aetiology of the Outbreak.

The aetiology of the disease was also remarkable in that the outbreak was largely due to two organisms. This in itself was of interest, since outbreaks of tinea corporis are commonly due to a single dermatophyte.

Of these two organisms, *E. floccosum* caused a proportion of the intertriginous lesions; at the same time it showed a tendency to disseminate over the trunk and limbs. It has already been noted that dissemination of lesions due to *E. floccosum* is occasionally seen in temperate climates, so that there is no reason to think that the organism had departed in Malaya from its

typically anthropophilic (Wise and Sulzberger, 1938) pattern of behaviour. However, its association on a large scale with the typically zoophilic *T. mentagrophytes* is apparently unique.

The only other example of widespread body ringworm due to *T. mentagrophytes* which we have been able to trace is that described by Pautrier and Rietman (1922). The cases described by Fischer (1917) and Gutmann (1919), although probably due to *T. mentagrophytes*, were relatively few and occurred only sporadically.

The description of Pautrier and Rietman (1922) suggests that their *T. granulorum* was probably identical with *T. mentagrophytes*. They observed 100 cases of infection with this organism among patients in a mental hospital who were undergoing hydrotherapy. The lesions were multiple, often intertriginous and "epidermophytic" and did not suppurate. Two years later, however (Pautrier and Rietman, 1924), several cases with suppurating follicular lesions were noted. In this instance the organism evidently departed from its usual tendency to infect hair follicles and became capable of infecting glabrous skin as well. A similar change was seen in Malaya; this may be a natural development whenever infection occurs on a sufficiently large scale.

As Table V shows, the predominance of *T. mentagrophytes* and *E. floccosum* on the body was reflected in the species-distribution of organisms isolated from the feet. *E. floccosum* is, of course, well known as a cause of tinea pedis, but *T. mentagrophytes* has probably only rarely been isolated from the feet in the past. Because of diversity of nomenclature it is difficult to be certain on this point. Until recently it was customary to distinguish between *T. interdigitale* (or *E. interdigitale*) and *T. mentagrophytes* (or *T. gypsum*); but the matter has since been confused by the assumption that these two organisms are identical, the names *T. gypsum* or *T. mentagrophytes* being used to include both of them (Peck *et al.*, 1944; Ajello *et al.*, 1945; Hopkins *et al.*, 1947). Where the distinction is upheld (Muskatblit, 1933; Walker, 1950), *T. interdigitale* is found to be common as a cause of tinea pedis and *T. mentagrophytes* very rare. We believe, therefore, that ours is the first report of frequent and regular recovery of *T. mentagrophytes* from lesions of the feet.

The Apparent Replacement of T. interdigitale by T. mentagrophytes as a Cause of Tinea pedis.

The prevalence of *T. mentagrophytes* in Malaya seems to have been accompanied by a corresponding diminution in the importance of *T. interdigitale* as a cause of tinea pedis. This is well shown in Table VII, which compares the species distribution of foot infections in our series with the distribution found by Walker (1950) in her series of 39 cultures from the feet of Army recruits in England.

TABLE VII.—*Species Distribution of Foot Infections Found in this Series and by Walker (1950).*

	Number of infections.	<i>T. menta-</i> <i>graphytes.</i> %	<i>T. inter-</i> <i>digitale.</i> %	<i>T.</i> <i>rubrum.</i> %	<i>E. floccosum.</i> %
This series . . .	96	40·6	11·5	3·1	44·8
Walker (1950) . .	39	0	74·4	11·3	15·3

It can be seen that among young men entering the Army in the United Kingdom in 1948, *T. interdigitale* was a common cause of tinea pedis and *T. mentagrophytes* an uncommon one, whereas among British soldiers in Malaya and Hong Kong in 1947-48 the reverse was the case. If it can be assumed that before they went to the Far East the men we studied had a similar pattern of fungus infection to that observed in recruits by Walker (1950), it follows that a striking change in this pattern must have occurred during our subjects' stay in the tropics.

A possible explanation of this change, which no doubt goes far to explain most of the observed facts, is that men drafted to the Far East continually acquired *T. mentagrophytes* infections from those who had arrived there before them and had themselves been infected by their predecessors. The fact that most units were maintained at full strength by the introduction of small numbers of newcomers to replace those returning on leave or for demobilization supports such a view.

There is, however, an alternative explanation, namely, that in certain instances *T. interdigitale* was transformed into *T. mentagrophytes*, a possibility long ago envisaged by Weidman (1926). The prevalence of *T. mentagrophytes* and its adaptation to the feet could well be explained by such a transformation. We failed to find unequivocal evidence of this, but the following observation is suggestive. A unit of some 800 men was moved as a whole from England to Malaya. The men were not examined by us on their arrival at Singapore, but the medical officer of the unit stated that at that time there were no cases of body ringworm. The unit was sent straight to a new camp in Malaya, having a minimum of contact with other troops; three months later one of us examined an unselected sample of 200 men for evidence of skin disease. Body ringworm was found in 34%; many cases showed suppurating follicular lesions, which were almost certainly due to *T. mentagrophytes*. It is obviously impossible to exclude infection with *T. mentagrophytes* from sources already in Malaya; but if a transformation of *T. interdigitale*, present on the feet of these men when they left the United Kingdom, into *T. mentagrophytes* were postulated, the rapid spread of trichophytic ringworm in this unit is more easily explained.

As yet there is no clinical or experimental proof that such a transformation can occur. The observations recorded here suggest that Malaya would be a profitable field for further work on this problem.

SUMMARY.

- (1) An outbreak of fungus infections of the skin is described, affecting British troops serving in Malaya and Hong Kong.
- (2) The most striking feature of the outbreak was the high incidence of body ring-worm (33.5% of 1424 men).
- (3) *T. mentagrophytes* was recovered with unusual frequency from the body and the feet.
- (4) The remaining infections were due chiefly to *E. floccosum*, but also to *T. rubrum* and *T. interdigitale*.
- (5) The possible causes of the high rate of infection by *T. mentagrophytes* are discussed.

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ISONICOTINIC ACID HYDRAZIDE IN THE TREATMENT OF CUTANEOUS TUBERCULOSIS: PRELIMINARY REPORT.

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ISONICOTINIC acid hydrazide is the latest chemotherapeutic agent for the treatment of tuberculosis. It has already become well known for its action on pulmonary, meningeal and abdominal tuberculosis and a considerable volume of literature has accumulated on this subject, but information regarding its action on cutaneous tuberculosis is meagre. The only reference available in this country at the present time is that of Grütz (1952). He reported excellent results achieved in cutaneous tuberculosis with isonicotinic acid hydrazide—results more impressive than those obtained with calciferol.

In order to test this method of treatment a series of cases of lupus vulgaris and tuberculosis verrucosa cutis, selected from the Skin Clinic of the Calcutta School of Tropical Medicine, were treated with the drug. The patients were of either sex and of ages varying between 4 and 42 years with histories ranging from 8 months to 15 years: lesions varied from small solitary ones to multiple and extensive granulomatous disease.

The diagnosis was made on clinical grounds and confirmed in some cases by histopathological examination of biopsy material. Mantoux's test was done in all cases with uniformly positive reaction: Wassermann reaction and Kahn tests were negative in all cases except one. Skiagrams of the lungs were performed as a routine procedure, and cases showing concomitant pulmonary tuberculosis were excluded. E.S.R. (Wintrobe) determined in a few cases was high, varying from 30–45 mm. in 1 hour. Urine examination did not reveal any abnormality in any case. Body weights of the patients were also recorded before commencement of treatment.

The full details of the series of 36 cases treated with 100–150 mg. daily for a period varying from 4–19 weeks are presented in the following tables.

RESULTS.

Of the 36 cases treated 21 were completely cured (Table I); two cases improved to a great extent, but became resistant to this form of therapy after

TABLE I. Continued.

No.	Age (years).	Sex.	Type.	Site and size of lesions.	Duration (years).	Previous treatment.	Treatment with isonicotinic acid hydrazide.	Toxic symptoms.
1	30	F.	Lupus vulgaris	Right palm, $2'' \times 1\frac{1}{2}''$	9	<i>Nil</i>	25 mg. 4 times daily for 5 days; later, 50 mg. <i>t.d.s.</i> Total, 5000 mg. in 5 weeks	<i>Nil.</i>
2	18	M.	"	Right knee, $3'' \times 2\frac{1}{4}''$	5	"	50 mg. <i>t.d.s.</i> Total 8750 mg. in 8½ weeks.	"
3	21	M.	T.V. cutis	Base of left big toe, $1'' \times 1\frac{1}{2}''$	1½	"	25 mg. 4 times daily for 7 days, subsequently 50 mg. <i>t.d.s.</i> for 5 weeks. Total, 5000 mg. in 6 weeks	"
4	16	F.	"	Left sole, $3\frac{1}{2}'' \times 2\frac{1}{2}''$	3	"	50 mg. <i>t.d.s.</i> Total, 5000 mg. in 5 weeks	"
5	29	M.	"	Left sole, $2\frac{1}{2}'' \times 2\frac{1}{2}''$	2	"	50 mg. <i>t.d.s.</i> Total, 10,000 mg. in 10 weeks	"
6	18	M.	"	Base of right big toe, $1'' \times 1''$	8	"	50 mg. <i>t.d.s.</i> Total, 15,000 mg. in 15 weeks	"
7	21	M.	"	Left big toe, $1'' \times 1\frac{1}{2}''$	4	"	50 mg. <i>t.d.s.</i> for 1 month, and later <i>b.d.</i> for 7½ weeks. Total, 9700 mg. in 12 weeks	"
8	21	F.	Lupus vulgaris	Right side of chest, $4'' \times 4''$	5	"	50 mg. <i>t.d.s.</i> Total, 6000 mg. in 6 weeks	"
9	11	F.	"	Extensive lesions on the neck, left axilla, buttocks, left thigh, right side of the face	8	Calciferol 300,000 i.u. bi-weekly, 35 injections I.M. at irregular intervals. Complete cure could not be effected	25 mg. <i>t.d.s.</i> Total, 2500 mg. in 5 weeks	Giddiness.
10	15	M.	"	(1) Left thigh, $1\frac{1}{2}'' \times 2\frac{1}{2}''$	4	<i>Nil</i>	25 mg. 4 times daily. Total, 9100 mg. in 13 weeks	<i>Nil.</i>
11	25	M.	"	(1) Front of right thigh, $5'' \times 4''$ (2) Lateral aspect of right thigh, $4'' \times 2\frac{1}{2}''$	5	"	50 mg. <i>t.d.s.</i> Total, 14,500 mg. in 14 weeks	"
12	12	F.	"	Left knee, $3\frac{1}{2}'' \times 4\frac{1}{2}''$	5	"	25 mg. <i>t.d.s.</i> Total, 5000 mg. in 9½ weeks	"
13	21	F.	"	Right buttock, $5\frac{1}{2}''$ diameter	9	Streptomycin 24 g. and PAS 1000 g. Much improved but not totally cured	25 mg. 4 times daily for 15 days, followed by 50 mg. <i>t.d.s.</i> for 10 weeks. Total, 12,000 mg. in 12 weeks	"
14	13	F.	"	Left buttock, $3\frac{1}{2}'' \times 1\frac{1}{2}''$	6	<i>Nil</i>	25 mg. 4 times daily. Total, 4000 mg. in 6 weeks	"
15	42	M.	"	Lateral side of the left leg, $2\frac{3}{4}'' \times 1\frac{1}{2}''$	1½	"	50 mg. <i>t.d.s.</i> Total, 10,500 mg. in 10½ weeks	"
16	30	M.	"	Dorsum of the left foot, $\frac{3}{4}'' \times 1''$	2½	Penicillin, terramycin and sulphadiazine no effect. Ostein fort. 20 tab. Improved slightly, but medication had to be stopped due to intolerance of the drug	50 mg. <i>t.d.s.</i> Total, 10,000 mg. in 10 weeks	"
17	24	F.	"	Right knee, $3\frac{1}{2}'' \times 4\frac{1}{2}''$	15	<i>Nil</i>	50 mg. <i>t.d.s.</i> Total, 9750 mg. in 9½ weeks	"
18	20	F.	"	Left side of the face. Few nodules on the healed lesion.	5	Cured with calciferol 600,000 i.u. bi-weekly, 35 injections. Relapse after one year.	25 mg. 4 times daily. Total, 5000 mg. in 7 weeks.	"
19	28	M.	T.V. cutis	Left sole, $3'' \times 2\frac{1}{2}''$	8	Calciferol 600,000 i.u., 45 injections. Streptomycin 1 g. <i>b.d.</i> , total 12 g. Novophone 50 mg. tab. <i>b.d.</i> 35 tab.	50 mg. <i>t.d.s.</i> Total, 5000 mg. in 5 weeks	"
20	18	M.	Lupus vulgaris	(1) Right axilla, $3\frac{1}{2}'' \times 6''$ (2) Right arm, $\frac{1}{2}'' \times 2\frac{1}{2}''$	3	<i>Nil</i>	50 mg. <i>t.d.s.</i> Total, 5000 mg. in 5 weeks	"
21	12	M.	T.V. cutis	Right ring finger, $\frac{1}{2}'' \times \frac{3}{4}''$	2	"	25 mg. <i>t.d.s.</i> Total, 3150 mg. in 6 weeks	"

Cases Resistant to Isonicotinic Acid Hydrazide, Later Cured with other Anti-Tuberculous Drugs.

No.	Age (years).	Sex.	Type.	Site and size of lesion.	Duration (years).	Previous treatment.	Treatment with isonicotinic acid hydrazide to date (still continuing).	Toxic symptoms.	Results and conclusions.
1	6	M.	Lupus vulgaris	Back of the thigh, 2" diameter	2	Nil	25 mg. <i>b.d.</i> Total, 6000 mg. in 17½ weeks.	Nil	Results and conclusions. Almost cured. Ditto
2	26	M.	T.V. cutis	Right sole, 4" x 3½"	4	"	50 mg. <i>t.d.s.</i> Total, 18,900 mg. in 18 weeks	"	"
3	14	M.	Lupus vulgaris	Right knee, 3½" diameter	8	"	25 mg. <i>b.d.</i> for 2 days, then <i>t.d.s.</i> Total, 8350 mg. in 16 weeks	"	"
4	6	M.	Ditto	Right knee, 1½" x 1"	8	"	16½ mg. <i>t.d.s.</i> Total, 1000 mg. in 3 weeks	"	"
5	16	F.	"	Left buttock, 3" diameter	14	"	50 mg. <i>t.d.s.</i> Total, 7500 mg. in 7½ weeks	"	"
6	25	M.	T.V. cutis	Right sole, 3½" x 1½"	2	"	50 mg. <i>t.d.s.</i> Total, 12,000 mg. in 11½ weeks	"	"
7	4	F.	Lupus vulgaris	Two lesions on right buttock	3	"	12½ mg. in 11½ weeks	"	"
8	12	F.	Ditto	Extensive lesions on the right buttock, right thigh and knee	11	Calciferol 600,000 i.u., 8 injections. Some improvement	4500 mg. 4 times daily. Total, 25 mg. <i>t.d.s.</i> Total, 6000 mg. in 11½ weeks	"	"
9	35	M.	T.V. cutis	Right sole, 4" x 2½"	15	Nil	50 mg. <i>t.d.s.</i> Total, 6000 mg. in 11½ weeks	"	"
10	13	M.	Lupus vulgaris	Right buttock, 2½" x 3"	3	"	50 mg. <i>t.d.s.</i> Total, 11,250 mg. in 10½ weeks	"	"
11	26	M.	T.V. cutis	Left sole, 2½" x 1"	10	"	50 mg. <i>t.d.s.</i> Total, 10,500 mg. in 10 weeks	"	"
12	5	M.	Lupus vulgaris	Buttocks and left palm. Nodules reappeared on healed lesions	5	Calciferol 300,000 i.u., 10 injections. Streptomycin 4 g. <i>b.d.</i> , total, 15 g. PAS 1000 g. Cured. Relapsed and treated with streptomycin. No change	25 mg. <i>t.d.s.</i> Total, 3225 mg. in a little over 6 weeks	"	"

TABLE III.—Cases Still under Treatment.

No.	Age	Sex	Site and size of lesion.	Duration (years).	Previous treatment.	Treatment with isotonic acid hydrazide to date (still continuing).	Toxic symp- toms.	Results and conclusion.
1	6	M.	Lupus vulgaris	Back of the thigh, 2" dia- meter	2	Nil	25 mg. b.d. Total, 6000 mg. in 17½ weeks.	Nil
2	26	M.	T.V. cutis	Right sole, 4" x 3½"	4	"	50 mg. t.d.s. Total, 18,900 mg. in 18 weeks	" Almost cured.
3	14	M.	Lupus vulgaris	Right knee, 3½" diameter	8	"	25 mg. b.d. for 2 days, then t.d.s. Total, 8350 mg. in 16 weeks	" Ditto
4	6	M.	Ditto	Right knee, 1½" x 1"	8 months	"	16½ mg. t.d.s. Total, 1000 mg. in 3 weeks	" "
5	16	F.	"	Left buttock, 3" diameter	14	"	50 mg. t.d.s. Total, 7500 mg. in 7½ weeks	"
6	25	M.	T.V. cutis	Right sole, 3½" x 1½"	2	"	50 mg. t.d.s. Total, 12,000 mg. in 11½ weeks	" Improving slowly.
7	4	F.	Lupus vulgaris	Two lesions on right but- tock	3	"	12½ mg. 4 times daily. Total, 4500 mg. in 13 weeks.	" Improving rapidly
8	12	F.	Ditto	Extensive lesions on the right buttock, right thigh and knee	11	Calciferol 600,000 i.u., 8 in- jections. Some improve- ment	25 mg. t.d.s. Total, 6000 mg. in 11½ weeks	" Markedly improved.
9	35	M.	T.V. cutis	Right sole, 4" x 2½"	15	Nil	50 mg. t.d.s. Total, 11,250 mg. in 10½ weeks	" Improving slowly.
10	13	M.	Lupus vulgaris	Right buttock, 2½" x 3"	3	"	50 mg. t.d.s. Total, 10,500	" Much improved.
11	26	M.	T.V. cutis	Left sole, 2½" x 3"	10	"	50 mg. t.d.s. Total, 6000 mg. in 7 weeks	" Improving slowly.
12	5	M.	Lupus vulgaris	Buttocks and left palm. Nodules reappeared on healed lesions	5	(calciferol 300,000 i.u., 10 in- jections. Streptomycin 4 g. b.d., total 15 g. PAS 1000 g. Cured. Relapsed and treated with strepto- mycin. No change	25 mg. t.d.s. Total, 3225 mg. in a little over 6 weeks	" Ditto.
13	7½	M.	Ditto	Left palm, left knee and buttock	3	(calciferol 300,000 i.u., 14 in- jections: no beneficial effect. Streptomycin 4 g. b.d.; total 20 g. PAS 1400 g. Cured	25 mg. b.d. Total, 4000 mg. in 11½ weeks	" Improving rapidly.

1½ and 19 weeks and were finally cured with calciferol (Table II). The remaining 13 cases are still under treatment ; 3 are nearly cured, 6 improving quite rapidly and 4 are improving rather slowly (Table III).

Isonicotinic acid hydrazide showed practically no toxicity at the dosage used (100–150 mg. daily) up to a maximum period of 19 weeks. A mild reaction with nausea, loss of appetite, abdominal discomfort, constipation, uridiness, thirst and headache was observed in 2 cases only towards the end of the treatment : these symptoms did not necessitate withdrawal of the drug, and subsided spontaneously.

There was practically no variation of the body weight and of the E.S.R. before and after treatment.

CONCLUSION.

It may be concluded from the results of our study and investigation that isonicotinic acid hydrazide is a very effective drug in cutaneous tuberculosis. It is cheap, easy to administer, and without any notable toxicity. In most of the cases the improvement was dramatic : the beneficial effect of treatment was noticed within 10–14 days and even earlier in some.

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ROYAL SOCIETY OF MEDICINE

SECTION OF DERMATOLOGY.

President—Dr. G. B. DOWLING.

18 December 1952.

Six Cases of Lupus Vulgaris Treated with Isoniazid.—Drs. G. B. DOWLING, E. WADDINGTON, R. G. HOWELL and D. L. REES.

Case I.—Mrs. O. B—, aged 51.

History.—The lupus began on the left cheek at 1–2 years, gradually spreading.

She had numerous treatments, including :

1935 : Radium plaque.

1938 : Finsen light.

1944–46 : Calciferol.

1946 : Skin grafting carried out successfully.

Since then the lesions remained inactive until June 1952, when she was found to have an active lupus nodule in the lobe of the left ear.

Treatment.—She was given isoniazid :

200 mg. daily for two months.

300 mg. daily for one month.

200 mg. daily for two months.

On 300 mg. daily she felt unwell and the dose was reduced to 200 mg. After two months the nodule was softer and after three months it had flattened considerably. It had disappeared after four months' treatment.

Case II.—Mr. C. L—, aged 44.

History.—In 1942 he attended Hospital with a twenty-year history of lupus vulgaris affecting the right side of the nose and upper lip. There was no mucosal involvement. In 1942 Eulykol injections produced considerable improvement.

In 1944 calciferol therapy was begun but the patient only attended for two months.

He was not seen again until August 1952 when he had numerous infiltrated nodules on the tip of the nose extending on to the upper lip and right naris.

Treatment.—August 1952 : Isoniazid 400 mg. daily started. After four months' treatment the nodules have disappeared and there is minimal scarring. There were no toxic effects.

Case III.—Mr. E. S—, aged 40.

History.—Single area of lupus vulgaris. This started at the age of 7 at the outer angle of the left orbit.

The origin of the adjacent sinus is thought to have been an inflammation, possibly tuberculous in origin, of the underlying bone. A skiagram revealed no underlying bone changes.

1941 : Radium plaque applied.

June 1951 to April 1952 : Calciferol therapy with partial regression, and some flattening only.

Treatment.—He was then put on a course of isoniazid, when some improvement was noted within a month. This was progressive, and resulted finally in complete flattening of the plaque of lupus to give the present appearance with little if any clinical evidence of activity.

Dosage.—At first 250 mg. once a day of isoniazid, then increasing to 250 mg. twice a day. There were no toxic effects.

Duration of treatment.—Seven months.

Case IV.—I. C—, female, aged 44.

History.—Thirty years' history of lupus vulgaris affecting "chin-strap" of neck.

Calciferol therapy began in 1946 and continued with rest periods until March 1948.

At this time there were no signs of clinical activity.

In August 1952 she presented again with numerous nodules in the scar.

Treatment.—Isoniazid 200 mg. daily for two weeks and then 300 mg. daily for two months. There was great improvement after six weeks. All the nodules had flattened and scaling had occurred. After four months' treatment there are one or two pigmented macules in the scar. No toxic effects.

Case V.—L. H—, female, aged 63.

History.—Duration of lupus vulgaris on the left cheek: forty-seven years. She was first seen in 1944, when she had an irregular scarred area on the left cheek with nodules at the edge and in the centre of the scar.

Treatment.—June 1944 to July 1950: Calciferol therapy with rest periods. She never developed signs of toxicity nor was there much improvement.

July 1950: Streptomycin and PAS. After a six weeks' course there was slight flattening of the nodules.

August 1951 to May 1952: Thiosemicarbazone 200 mg. daily. After two months' treatment there was some improvement, but despite continued treatment new nodules appeared in the centre of the scar.

June 1952: Isoniazid given with a dosage of 200 mg. daily for the first two months, and then 300 mg. daily for a further two months.

Progress.—After one month all the nodules had flattened and their surfaces became scaly. Improvement was maintained. After fifteen weeks' treatment she developed erythema nodosum on both lower legs and simultaneously the left cheek became swollen and red. Treatment was stopped, and this reaction subsided in three weeks. The lupus vulgaris appeared to be clinically inactive and only pigmented macules were present in the scarred area. She has had no treatment for the past two months. There have been no signs of toxicity.

Case VI.—Mrs. M. M—, aged 67.

History.—Large sheet of lupus starting in childhood and involving the right side of the face.

Intermittent treatment with calciferol since 1946. This had to be discontinued on several occasions because of nausea and vomiting and urinary symptoms. The lupus improved, but many active nodules persisted in the scar.

Treatment.—Course of isoniazid: At the beginning of treatment a crop of raised lupus nodules was scattered throughout the scar tissue. Response was rapid; at the end of four months' treatment no infiltrated nodules remained and only a few pigmented macules were present. No toxic effects. Dosage: 300 mg. daily.

Comment.—We have presented 6 out of 15 cases of lupus vulgaris that have been treated for at least four months with isoniazid. Of these 15 cases all except one had previously received calciferol for a prolonged period and had either relapsed or had proved resistant to the treatment. Some had also been treated in addition with streptomycin and with thiosemicarbazone. The dosage of isoniazid was initially 3 mg. per kg. body-weight per day, but after two months this was increased to 6 mg.

Results.—All the cases, with the exception of one patient on whom treatment was abandoned because of toxic effects, showed striking improvement within one month. Nodules arising in scarred areas rapidly flattened. After four months' treatment only 2 cases showed any clinical evidence of activity.

Toxicity.—Toxic effects occurred in 4 patients. One patient developed severe vertigo and a coarse tremor of the hands within a week. After a rest of two weeks a dose of 50 mg. per day was tried but the symptoms returned and treatment was abandoned.

The second patient developed extreme fatigue and numbness of the head after two months' treatment with a dose of 3 mg. per kg. Her lupus was at that time clinically inactive and treatment was stopped. She has been followed for a period of three months and no relapse has occurred.

The third patient developed fatigue and an enormous appetite and put on a stone in weight after being treated for seven weeks. The lupus has improved but there are still signs of activity.

The fourth (Case V) developed erythema nodosum on the legs and swelling and congestion of the lupus area after fifteen weeks' treatment. This reaction subsided within three weeks and the lupomata have flattened, leaving pigmented macules in the scar.

Lupus Vulgaris Treated with Isoniazid.—Dr. G. B. DOWLING and Dr. R. H. SEVILLE.

A. F—, male, aged 37.

History.—For the past twenty-one years the patient has had a slowly growing area of lupus vulgaris of the skin over his epiglottis. Ten months ago he noticed a lump in his hard palate, and biopsy at the Institute of Dental Surgery showed this to be lupus. Mr. D. Downton therefore referred him to St. John's Hospital for treatment.

1912: Small area of lupus on the lower part of left leg, clearing with "blue ointment" in one and a half years. 1929: Area of lupus vulgaris under chin "following blow on tuberculous gland of neck" one year previously. Lesion cleared; cauterized and general ultraviolet light given for six months. 1931: Patient noticed onset of lesion over epiglottis (*vide supra*). 1937: Abscess left buttock and outer right thigh, leading to the diagnosis of tuberculous spine.

On examination.—A typical lesion of lupus could be seen over the epiglottis measuring 3.8×3.8 cm. Under the chin there was a scarred area of older lupus which contains active nodules. On the right side of the hard palate a brown infiltrated area was present measuring 0.3×0.6 cm.

Special investigations.—X-ray chest: shows adhesions at the right lung base and a healed calcified shadow in the left middle zone. There is no evidence of any active lung disease.

Mantoux: 1:10,000 negative. 1:1000 positive.

Treatment.—Treatment with isoniazid (100 mg. *t.d.s.*) was started six months ago. All the active lesions looked paler and flatter at the third week. After six weeks' therapy there were no signs of the palatal lesion and only a few ghost lesions could be seen on the neck. These latter have disappeared following a three months' course of calciferol (100,000 i.u. daily) and a further six weeks' isoniazid (150 mg. three times daily).

Comment.—Calciferol was given as an alternative therapy, as it was thought that the tendency for developing drug resistance would be reduced by limiting the length of the courses.

The PRESIDENT: We have shown these cases with the intention of comparing notes.

In addition to the 15 cases so far treated at St. Thomas's, 4 in-patients have been treated at the Morland Clinics at Alton, 2 previously untreated and 2 old cases which had been treated both locally and with calciferol. All 4 were clinically cured within less than four months, that is, none of the characteristic lupomatous nodules can now be seen. One case of severe senile tuberculous adenitis with multiple discharging sinuses, treated in the out-patient department at St. Thomas's Hospital, has cleared completely in about the same period.

The speed and reliability of this treatment have greatly exceeded that of calciferol and of calciferol combined with streptomycin, while with thiosemicarbazone we never achieved any striking degree of success. We are now abandoning treatment for new cases with isoniazid alone in favour of the treatment advocated by Joiner and others (1952, *Lancet*, 2, 843), that is, the combination of isoniazid and streptomycin.

Dr. BRIAN RUSSELL and Dr. N. A. THORNE :

Progress Report on 15 Cases.

Dr. BRIAN RUSSELL: We wish to make a progress report on 15 patients who have been treated with isoniazid for periods varying between nine and thirty weeks. We have adopted strict criteria of improvement—it is only permissible to contemplate the possibility of "cure" of lupus after all physical signs of activity have been absent for at least five years. After clinical cures from all forms of treatment used up to the present, biopsies have sometimes revealed the presence of tubercles in apparently healed areas. Time alone can tell whether isoniazid will prove the exception by removing histological as well as clinical evidence of tuberculosis.

In our trial, then, clinical clearance is taken to mean the disappearance of all redness, infiltration, scaling and "apple-jelly" nodulation. If the faintest scaling or brownish discoloration remains at the site of the nodule progress has been described as marked (3+). If there is slight residual infiltration, with scaling and increased opacity of the lesions the grading has been moderate improvement (2+). Slight improvement (1+) implies a diminution of redness, infiltration, scaling and translucency. All observations of progress have been controlled by photographs, using the same factors of lighting, exposure, etc., throughout.

The minimal reasonably effective dose for an adult seems to be 100 mg. three times a day, and we have given 100 mg. four times a day to some patients who have not responded well enough to the smaller dosage. We have given the drug orally or by local intralesional injections or by a combination of these methods. With oral treatment a steady and quiet improvement takes place, without early exacerbations such as are often observed with calciferol. The effect of isoniazid seems to be on the organisms and that of calciferol on the host, and there seems no reason why the two treatments should not be given together if desired.

Dr. N. A. THORNE: I will describe a few illustrative cases:

Case 1.—A woman, aged 47, had suffered from lupus vulgaris for eight years. She had been treated previously with carbon arc baths and the Finsen-Lomholt lamp; the latter had caused severe reactions with only slight improvement. After twenty-seven injections of 50–100 mg. isoniazid weekly there was moderate improvement (2+).

Case 2.—Woman, aged 52, shown to this Section in April 1952 on behalf of Dr. W. J. O'Donovan. Her extensive lupus of the face and neck had remained untreated for over thirty years. She was given isoniazid by mouth 300 mg. daily and daily carbon arc baths to the trunk and the face and limbs only, the neck being shielded from the light rays. Before treatment there were closely packed raised nodules surrounded by a purplish-red discoloration, erythema and considerable scaliness. After thirty weeks much of the erythema had been replaced by pigmentation, and although active nodules with scaliness still persisted on the pinnae and over the angles of the jaw, there was almost complete flattening of nodules and absence of scaliness over the greater part of the face, and discrete nodules over the shoulders had been replaced by pigmented scars. Improvement marked (3+).

Case 3.—Man, aged 48, with surgical ankylosis of one knee-joint following tuberculosis. He had suffered from lupus for thirty-four years, the right side of nose, "chin-strap" area, occiput and palate being affected. Light treatment had been used with success in the past but relapse had recently occurred. Isoniazid 300 mg. daily was given for eighteen weeks and at this time all lesions were regressing, nodules becoming flatter and scaliness disappearing. Improvement moderate (2+).

Case 4.—Woman, aged 51, with lupus of ten years' duration which had been treated with ultra-violet rays and with calciferol. She developed pulmonary tuberculosis, which had become quiescent following rest, streptomycin and PAS. The lupus responded poorly to all these remedies, and it was decided to give isoniazid by local injection lest its oral use might produce drug-fast organisms and so detract from its possible future value in the control of the chest condition. Nineteen weekly local injections of from 50–250 mg. of isoniazid were given into the active lupus over the right elbow, without any definite improvement. This was our only complete failure by either method of administration of isoniazid (No change).

Case 5.—Man, aged 31. He had a nephrectomy four years ago for unilateral renal tuberculosis. Lupus first occurred twenty-seven years ago. Ultraviolet rays had cleared one lesion behind the left knee but active nodules remained amidst scar tissue above the right patella. Following twenty-six weekly injections of isoniazid locally the nodules had become much flatter, scaliness had disappeared and all local pain and discomfort had ceased. This was the only case under review to develop any complication—a mild degree of urticaria which did not interfere with continuation of the injections. Improvement moderate (2+).

Case 6.—Man, aged 36. He had suffered from lupus over the left popliteal fossa for thirty-four years, and had been irregular in his attendance for treatment with the Finsen-Lomholt lamp. He responded moderately well (2+) to weekly local injections of 50–250 mg. of isoniazid but the spread of lupus at an uninjected site made oral treatment necessary. Improvement moderate (2+).

Case 7.—Woman, aged 46. She had suffered from lupus for twenty-nine years. When first seen the two lesions in the region of the right knee had a superimposed dermatitis medicamentosa due to penicillin cream which had been used to control a secondary infection. When the dermatitis

had subsided she was treated with isoniazid by mouth, 150–300 mg. daily. One of the lesions was also given local weekly injections of 100 mg. After twenty-nine weeks both lesions were rapidly clearing, more especially the one into which injections were given. An assessment of marked improvement was made (3 +).

SUMMARY OF RESULTS.

	Oral.	Local.	Oral and local.	Total.
Cleared	—	—	—	—
Marked (3 +) improvement	3	1	1	5
Moderate (2+) improvement	1	4	2	7
Slight (1 +) improvement	1	—	1	2
No change	—	1	—	1
Total	5	6	4	15

Local injections of comparatively small doses of isoniazid at weekly intervals produce clinical improvement which lags behind that achieved by oral therapy. A trial of daily injections has not been made because of patients' objections to daily visits to hospital, but it might prove as valuable as oral treatment in selected cases.

We are now trying out a combined treatment with calciferol and isoniazid.

Dr. J. SOMMERVILLE and Dr. J. A. MILNE :

Report on 26 Cases.

Dr. J. SOMMERVILLE : I have treated 26 cases with isoniazid (250 mg. per day) for periods of from seven to thirty-two weeks.

In only 1 of these 26 cases was there a suspicion of pulmonary involvement, but subsequent x-ray findings disproved any activity. In reports so far published on the treatment of pulmonary tuberculosis with isoniazid the average number claimed as clinically cured is 25% ; the M.R.C. report* confirms a distinct tendency in these cases to drug resistance, increasing from 11% at the end of the first month to 71% at the end of three months.

Of our 26 cases of skin tuberculosis not one has failed to show continued improvement : this apparent difference in response I am not able to explain. We claim 7 clinically cured and 8 almost so, the remainder showing varying degrees of progress.

Toxic effects have been noted in 5 cases ; 3 suffered from menorrhagia, in 2 there was lassitude and loss of appetite, and 2 had polyuria ; a few others showed increased appetite and one had an "almost pleasant sense of drunkenness."

Our results would seem to suggest that the drug is safe and efficacious.

Dr. John A. Milne, Lecturer on Skin Histopathology at Glasgow University, will report on the histopathological findings.

[Dr. Sommerville illustrated his remarks with photographs of 4 patients. Cases I and II had broken down again after improvement following calciferol, but after seventeen weeks' treatment with isoniazid they revealed no evidence of clinical activity. The third had been refractory to light therapy, streptomycin, calciferol and Sulphetrone, and the fourth had had no previous treatment ; these 2 had improved markedly after nineteen weeks' and twenty-five weeks' treatment respectively.]

Dr. JOHN A. MILNE : I have examined 14 of these cases histologically, 10 of which have been re-examined after varying periods of treatment. In all of them there has been evidence of regression of the lesion.

The first case illustrated by Dr. Sommerville shows a typical picture of lupus vulgaris before treatment (Fig. 1). Ten weeks after treatment (Fig. 2) shows a virtually normal skin, with a few areas of lymphocytic infiltration.

The third case, illustrated with facial lesions, showed the typical histology of lupus before treatment. Fig. 3 shows the histology after nineteen weeks' treatment. The follicle has been replaced by a dense mass of lymphocytes with central giant cells of the Langerhans type. This appearance is interesting, and is in contradistinction to the picture of progressive transformation to "sarcoid" as obtained by the late Dr. W. Freudenthal in cases of lupus treated with calciferol. We hope to take further biopsies from this case.

In the fourth case illustrated by Dr. Sommerville—a lady with extensive lesion of the forearm—a biopsy before treatment showed typical lupus vulgaris. Ten weeks after treatment a biopsy was taken from the periphery of the lesion where there were clinical signs of activity. The histological appearances were interesting. An area of rather hyaline necrosis was spreading out from the centre of the follicle and appeared to be destroying it. The significance of this change is not clear, but it is most unusual in lupus.

Dr. G. A. HODGSON : We have treated 8 or 10 cases of lupus vulgaris with isoniazid which have all improved, but not as dramatically as the cases we have seen portrayed at this meeting. The

* Medical Research Council (1952), *Brit. med. J.*, 2, 735.

most improvement was shown in a child of 5 who had had no previous treatment. In the older cases it was my impression that the lesions did move on Rimifon (Roche) (isoniazid) but they moved more quickly with Rimifon plus calciferol, and I think there may be a case for giving Rimifon, calciferol and streptomycin all together.

Dr. W. J. O'DONOVAN: This exhibition of cases makes it plain that the fight against tuberculosis is proceeding among dermatologists as energetically as among general physicians.

For a quarter of a century I have been impressed, in the Lupus Department at the London Hospital, with the great difficulty of assessing progress and finality in cases under treatment. I would affirm that I had been seeing lupus daily for five years before I felt confident in suspending treatment and to this day I recognize the tubercle bacillus as so subtle an antagonist that I see such patients yearly.

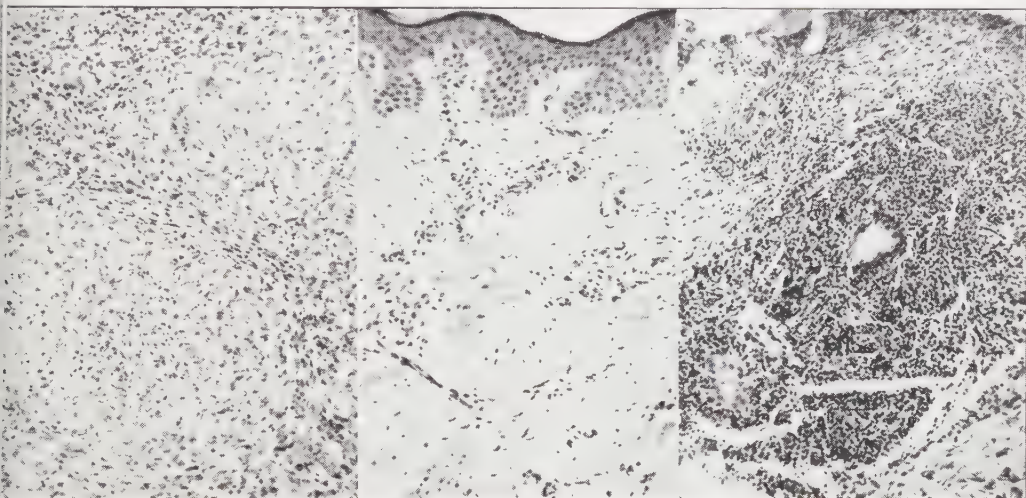


FIG. 1

FIG. 2

FIG. 3

FIG. 1 (*Case I*).—Typical lupus vulgaris nodule before treatment. $\times 100$.

FIG. 2 (*Case I*).—After ten weeks' treatment complete disappearance of lupus tissue. Fibrosis with minimal infiltrate. $\times 100$.

FIG. 3 (*Case III*).—After nineteen weeks' treatment (250 mg. daily). Illustrates unusual finding of replacement of epithelioid cells by lymphocytes. $\times 100$.

Time is a great factor in the estimation of cure. Speed in clearance does not give one certainty. When a face has been marked by treatment with acids, by scraping and by x-ray treatment a warning of the persistence of lupus is given by the presence of a very fine scale. This implies congestion perhaps well below the Malpighian layer.

If this be watched for six months there will appear a little, semi-translucent, bluish macule that needs treatment, or if left it becomes a recognizable early "apple-jelly" nodule.

Dr. LOUIS FORMAN: Isoniazid would appear to alter the skin reaction to the tubercle bacilli in the lupus granuloma. This may be more important than the antibiotic action. The bacilli are very scanty in lupus, almost impossible to demonstrate in sections, and difficult to culture. Again, we know that tubercle bacilli become resistant to isoniazid in about six weeks, but lupus vulgaris continues to improve with the drug during the treatment time of four months. Great care should be taken to exclude any active lung infection when using isoniazid for lupus vulgaris, for the general physicians believe that streptomycin should be given as well so as to delay the development of drug resistance.

The incidence of toxicity to isoniazid appears to be low but not insignificant. Thus two reports have described acute pellagra (McConnell, R. B., and Cheetham, H. D. (1952) *Lancet* 2, 959) and confusional psychosis with residual organic cerebral impairment (Hunter, R. A. (1952) *Lancet* 2, 960) following isoniazid treatment.

The PRESIDENT: The rate of progress of untreated lupus is determined by native and acquired resistance. Supposing that the cause, the tubercle bacillus, is even partially disposed of by chemotherapy, there is, I believe, no evidence that natural resistance is thereby lessened, or any reason for supposing that it cannot continue to exert an effect even beyond the time of

development of drug resistance. I feel strongly opposed to the view that because the disappearance of lupus from sight does not necessarily mean that it is permanently cured, therefore the new remedies are hardly worth trying. At the same time, I have always held to the view that local treatment remains an essential part of treatment.

The Treloar Hospital, Alton, has been equipped with Finsen and carbon arc lamps for many years: both here and at the Finsen Institute itself it has been admitted that until the advent of the new remedies, much widespread lupus could not be brought under control.

Primary Systematized Amyloidosis.—Dr. E. WADDINGTON.

Mrs. I. H—, aged 57.

History.—Six years ago the patient had to cease playing the clarinet owing to increasing thickness of her lips and fingers. For the past five years she has suffered from fatigue and has become aware of her changed facial appearance. Three years ago she first noticed increasing breathlessness on exertion, and during the last three months this has been severe and has been associated with swelling of the ankles. Two years ago her voice became husky. She has recently developed indigestion and flatulence and has had occasional attacks of diarrhoea.

On examination.—There is marked coarsening of the features, but no prognathism. The complexion is ruddy and the eyelids, lips and skin of the chin are thickened. The tongue is grossly enlarged and its movements are restricted. On palpation it has a rubbery consistency. The surface is normal. There are numerous purpuric spots on the chin and also on the buccal mucosa. The hands are broad, and there is a doughy thickening of the skin on the medial and lateral aspects of the fingers. This infiltrated area is light brown in colour and semitranslucent. There are a number of ecchymoses on the surface. The feet show similar but less severe changes. There is bilateral chemosis, and on the lateral aspect of the bulbar conjunctiva of the left eye there is a translucent nodule. (This lesion has been biopsied.) The heart is enlarged. The jugular vein is distended up to the angle of the jaw. There is oedema of the sacrum and ankles and crepitations at both lung bases. Blood-pressure 200/130. The liver edge is palpable 1 in. below the costal margin. There is thickening of both ulnar nerves.

Urine: Albumin ++. Epithelial cells. Repeated examination showed no Bence-Jones protein.

Investigations.—Skiagrams of the skeleton (including pituitary fossa) showed no evidence of bone disease. Skiagram of the chest showed an increased transverse diameter of the heart with congestion of the lungs.

Electrocardiogram: a low voltage curve with ventricular extrasystoles. Blood examination showed no abnormality. Serum proteins 5.4, albumin 3.1, globulin 2.3%. B.M.R. + 10%. Plasma cholesterol 182 mg. %.

Histology.—(1) *Skin from side of finger:* The connective tissue of the dermis is largely replaced by a coarsely fibrillary material. In this material there are numerous clefts, some looking like artefacts; others being lined by nuclei, resemble vascular spaces, but the presence of intermediate forms indicates that they are all of the same origin. Scattered among the masses of fibrillary material are deposits of fibrin.

The staining reactions of the fibrillary material are as follows:

Eosin, Congo red intravitaly, positive.

Van Gieson, Weigert's Elastic, Congo red in fixed tissues, negative.

Methyl violet, no metachromasia.

Reticulin, negative.

(2) *Nodule from conjunctiva.*—The biopsy shows similar changes to those in the skin. The appearances suggest that the "amyloid" material is an altered form of collagen rather than the deposition of any new substance. Morphologically it is unlike the material seen in true amyloidosis.

Comment.—Primary systematized amyloidosis may be distinguished from the more common form of secondary amyloidosis by the following features:

(1) It is not associated with chronic suppuration, granulomatous disease or rheumatoid arthritis.

(2) Metachromatic staining of the material is variable.

(3) The distribution of the amyloid is distinctive, with widespread involvement of muscle and small blood-vessels. Particular features are macroglossia, gastro-intestinal and cutaneous infiltration and heart failure.

Our patient was admitted with severe hypertensive cardiac failure, but in view of the changes in the electrocardiogram it is possible that amyloid infiltration of the cardiac muscle was a contributory cause. Despite improvement in her cardiac condition gross albuminuria persists, suggesting similar involvement of the renal vessels.

The patient closely resembles the case reported by Wells, G. C. (1952, *Brit. J. Derm.*, **64**, 169). His patient also showed an abnormal serum beta-globulin and an increase in plasma cells of the bone marrow, without any evidence of bone destruction. Wells discusses the significance of these findings, and suggests that this plasmocytosis is more likely to be a reactive phenomenon than a malignant myeloma. There is experimental evidence of a relationship between the production of antibodies and the number of plasma cells, and this plasmocytosis of the bone marrow, combined with an abnormal circulating globulin, suggest that primary amyloidosis should be classified with the disorders of immunity.

My thanks are due to Dr. H. K. Goadby for permission to show this case.

Borst-Jadassohn Intra-epidermal Epithelioma.—Dr. H. HABER and Dr. R. H. SEVILLE.

S. S—, male, aged 39.

For the past two years this patient has had a slowly growing brown papillomatous tumour on his left temple (Fig. 1). Clinically the lesion was like a seborrhoeic wart, but biopsy was undertaken because it was fleshy and had a firm edge.

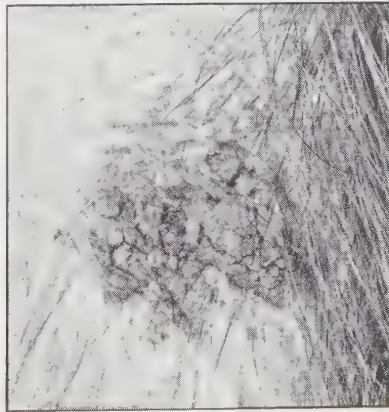


FIG. 1.—Papillomatous demarcated lesion of Borst-Jadassohn intra-epidermal epithelioma on the left temple. $\times 2$.

Histological section shows a verrucose lesion that has been produced by an irregular hyperplasia of the epidermis which has changed its whole architecture. The stratum corneum is increased and shows areas of parakeratosis which correspond with the absence of stratum granulosum in the same places. The stratum spinulosum shows two types of cells, darker staining spindle-shaped cells with a hyperchromatic nucleus exhibiting quite a number of mitotic figures. They are arranged in peculiar whorls. There is also intercellular oedema. The other type of cell shows homogenization of

its protoplasm and a more eosinophilic staining producing a picture as if the stratum spinulosum has been replaced by a basal-cell and squamous-cell epithelioma of low grade. It is a rather bizarre histology not seen in any other intra-epidermal epithelioma. The tumour is sharply defined, and the corium exhibits dilated blood-vessels and a round-cell infiltration (Fig. 2).

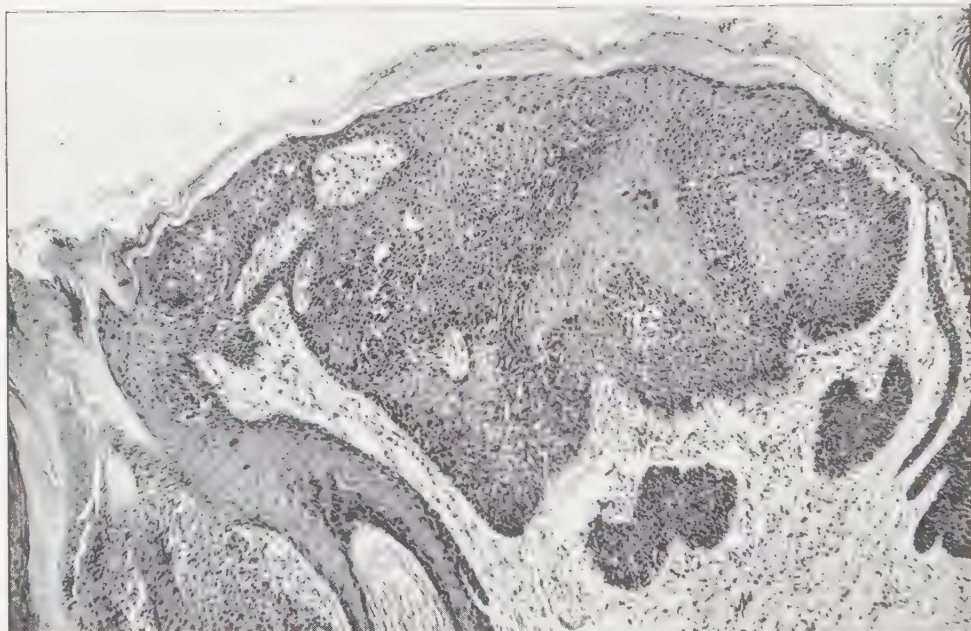


FIG. 2.—Intra-epidermal change. $\times 140$.

Dr. H. HABER: There are several types of intra-epidermal epithelioma met with in dermatological histology; Bowen's disease, Paget's disease, erythroplasia of Queyrat and intra-epidermal basal-cell epithelioma. For the last two or three years I have come across lesions appearing as solitary warty papules or plaques of a peculiar appearance suggesting epidermal naevi, cellular naevi, seborrhoeic warts or even melanomas. These could not be diagnosed clinically. The histology is of such a character that it must be regarded as a separate entity which was first described by Borst and forgotten but, later, attention was drawn to it by Jadassohn. The lesion shows peculiar disarrangement of the architecture of the stratum Malpighii with islands of spindle-shaped cells with prickles invading the epidermis, with a tendency to form whorls. In some places squamous cells or premature hornified cells can be seen behaving in the same manner. There appear to be basal-cell epitheliomas or squamous-cell epitheliomas within the epidermis. I have not yet come across a lesion which has penetrated through the basal layer to invade the corium; so that one cannot say if this is a true intra-epidermal epithelioma or some peculiar naevogenic malformation within the epidermis.

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Trichostasis Spinulosa with Histological Features of Lichen Spinulosus. — Dr. P. J. HARE.

M. M—, man aged 30, Cypriot.

History. This man came to this country two years ago. During this time he has noticed rough areas on the skin of the shoulders and back. These places itch in hot weather. He is otherwise perfectly well and eats a normal diet. His sister has also been in England for two years, but as far as he knows she has no disorder of the skin.

On examination.—The skin of the shoulders, upper arms, sides of the back, buttocks, upper abdomen and nose show dark brown areas about a millimetre in diameter through which project short hairs, producing a nutmeg-grater appearance. The lesions are diffusely scattered, and between them the skin and hair-follicles appear normal.

Investigations—Histology.—The lesions can be picked out: under the microscope they show bunches of lanugo hairs piercing horny plugs. Histologically, the follicles are widened and contain loose keratin and pieces of lanugo hair. Many follicles are invaded by epithelioid cells, lymphocytes and giant cells of the foreign-body type. There are also small areas of lymphocytic infiltration outside the follicles. Blood W.R. negative.

Comment.—This appears to be a case of *Trichostasis spinulosa* (Nobl). The histological picture closely resembles that depicted in Gans's text-book under *Keratosis spinulosa* (*Lichen spinulosus* of Crocker).

Since seeing this case similar lesions on the nose of a middle-aged Polish woman have been found to yield bundles of lanugo hairs similar in appearance to those in the above case.

This condition was given this name by Nobl in 1913. It was described independently by Galewsky, who thought it was rare. Nobl collected six cases within a few months. Other people have felt that it is common if looked for, but one feels some doubt about that. The histological information on this condition is rather scanty. Nobl gave some details in his paper, with pictures showing follicular dilatation, with a keratin plug block enclosing lanugo hairs. Hochstetter described buds coming off the end of each follicle and thought that these were forming a compound papilla.

In my case there is not much evidence of a compound papilla. It has a maximum of five or six hairs in a follicle, but it fits in with the general description of the condition. I am struck by the fact that the changes in the follicle appear to be similar to those depicted in Gans's textbook, under *Keratosis spinulosa*. I would welcome the views of the meeting on the possible origin and treatment of the condition. I thought of following the usual treatment of a keratotic condition, and watching to see how long it took to re-form the lesions.

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Dr. I. MARTIN-SCOTT: The histology shows a compound lanugo follicle with many more hair-shafts than there are hair papillae. This suggests that each individual papilla has formed several complete hairs, which have been arrested at the follicular ostium. Perhaps this blockage is due to a change in the keratin composition, but it may be due to lack of sebaceous lubrication. The sebaceous glands are absent or atrophic in this condition, yet normally lanugo follicles are well endowed with these glands.

In the comparable condition of ichthyosis with keratosis pilaris the sebaceous secretion is also diminished, and the lanugo hairs are not shed but curled up in a mass within the keratin plug.

It seems possible, therefore, that this loss of sebaceous secretion might account for the arrest of normal hair loss, and the neat sheaves of complete lanugo hairs seen in this rare condition of trichostasis spinulosa.

The PRESIDENT: I believe I showed the only other case of this condition that has been seen at these meetings in recent years (1946) *Brit. J. Derm.*, **58**, 6. From the literature on the subject that I was able to find at that time I understood that it was generally regarded as a late developmental abnormality in which the affected follicles possessed buds capable only of producing lanugo hairs which collected as a sheaf inside the main follicle.

Dr. P. J. HARE: Various views have been expressed. A recent report by Leider,* described *Trichostasis spinulosa* associated with trichorhexis nodosa and pili annulati. His patient's daughter also had ringed hairs, which suggested a genetic basis.

* LEIDER, M. (1950) *Arch. Derm. Syph., Chicago*, **62**, 510.

Vitiligo Treated with Mepacrine. Dr. J. S. PEGUM (for Dr. P. J. HARE).
Mrs. S—, aged 58.

The patient, who is of Italian origin, noticed white patches on the hand 14 months ago; later further patches appeared on the arms, trunk and thighs.

Previous diseases: 15 years ago developed bald patches in the scalp which spread until there was total alopecia of the scalp. The hair regrew spontaneously.

Five months ago a serous cystadenoma was removed and total hysterectomy and salpingo-oöphorectomy were done.

Examination (22.x.52.) The skin was of a warm olive tint. Areas of vitiligo were seen on the hands, arms, back, chest, abdomen, thighs and legs. There was an appearance of hyperpigmentation around the areas of vitiligo.

W.R. and Kahn negative.

Mepacrine was given by mouth in the following dosage:

24-29.x.52, 0.1 g. *b.d.*

29.x to 5.xii.52, 0.1 g. *t.i.d.*

5.xii to 12.xii.52, 0.1 g. *b.d.*

12.xii to 18.xii, 0.1 g. daily.

Present Condition.—The normal skin varies in colour from yellow to golden brown. The areas of vitiligo are apparently normal skin colour, but when examined through a white paper mask to eliminate the colour contrast of the surrounding skin the vitiliginous areas also are seen to have a yellow hue.

Examination under Wood's light.—The palms are intensely fluorescent. The normal skin is fluorescent to a lesser extent; the areas of vitiligo also fluoresce, those on the backs of the hands apparently to a greater extent than the surrounding skin, which shows the dark dappled "melanin" effect.

Comment.—Mepacrine was used following a similar observation on a patient of Dr. Forman's, who was given mepacrine as treatment for light sensitivity, and whose vitiligo, which had been scarcely visible before treatment, became prominent after a few weeks of mepacrine medication, apparently by accentuating the colour contrast. It was felt that this was the result of increase in melanin in the surrounding skin, and accordingly mepacrine was given in the present case in the hope that it would cause pigmentation to spread in from the borders of the depigmented areas.

Mepacrine appears to accentuate the colour contrast between the normal skin and the vitiliginous, since the vitiligo seems to be stained but little, while the surrounding skin is golden brown in colour. We have considered a number of explanations for this phenomenon.

1. That the mepacrine is taken up by the normal skin but not by the vitiliginous. This is the most obvious explanation, but it is not confirmed by investigation; since if a white mask is used to eliminate the colour contrast of the surrounding skin the vitiligo also is seen to be yellow; also examination with Wood's light shows that some of the vitiliginous areas actually fluoresce more than the normal skin. Further, biopsies of the normal and vitiliginous skin examined by fluorescence microscopy reveals no apparent difference in intensity of fluorescence.

2. That this is a purely optical effect. It is possible that mepacrine in the skin acts as a filter, and accentuates the colour contrast between normal and depigmented skin in the same way that a yellow filter in photography accentuates the contrast between cloud and sky. This would seem to provide at least a partial explanation, and it is my own subjective impression that viewing patches of vitiligo and surrounding skin through a yellow filter does produce an accentuation of the colour contrast.

3. That mepacrine administration results in an increase in the melanin in the skin, either by a local action on the melanoblasts, or by stimulating the pituitary to produce pigment hormone. The latter would provide an explanation for Page's observation (1951) that mepacrine by mouth raised the light erythema threshold.

while locally applied mepacrine did not. If mepacrine also stimulates the pituitary to produce ACTH this would account for the beneficial effects of mepacrine in acute lupus erythematosus and in rheumatoid arthritis. Mepacrine does not stimulate the melanophores to expand in the frog, but this does not preclude its having a pigmentotrophic effect in humans.

4. The fourth possibility is that mepacrine combines with melanin or its precursors in the skin to form a new compound.

As to the effect of mepacrine on vitiligo, the short-term effect at any rate is to make it worse by making it more obvious: this suggests that melanoblast stimulation, if it occurs, is confined to normal skin, so that there is a rise in background pigmentation, throwing the depigmented areas into relief in the same way as presumably occurs in Addison's disease and other pigmenting endocrine diseases.

REFERENCE.

PAGE, F. (1951) *Lancet*, **2**, 755.

Dr. F. RAY BETTLEY: This effect in vitiligo is one that Dr. Page and I have noticed in our cases. We noticed it very strikingly in a boy with golden hair and blue eyes and a very pale skin, so pale that one could not see any vitiligo until he was given mepacrine, when it became obvious at once. We have been cutting sections of the skin much as Dr. Pegum has done and with very much the same results; we have not reached any conclusion. I consulted a biochemist about the chemical side of it but he was unable to make any suggestion as to how mepacrine can be concerned with melanin or the production of melanin. It seems clear that the alteration in light sensitivity which takes place when patients are given mepacrine is not the result of increased melanin pigmentation.

Dr. DAPHNE ANDERSON: Mepacrine decreases light sensitivity, possibly partially because it causes fluorescence of the skin, thus converting ultra-violet to visible light. Curiously enough fluorescence of the skin can be caused by certain light sensitizers and light barriers, e.g., Aesculin, quinine, vaseline, ammoidin.

Dr. BETTLEY: We carried out the dopa reactions on biopsies of patients with lupus erythematosus and found that they were almost completely dopa-negative. That does not mean very much, for a healed patch after many disorders is rather pale, showing that there has been a suppression of melanogenesis. We thought this might have something to do with the effect of mepacrine.

The following cases also were shown:

Reticulo-Granuloma.—Dr. R. J. CAIRNS and Dr. H. HABER.

(1) **Necrobiosis Lipoidica (Non-diabetic Type) Treated by Excision and Grafting.** (2) **Case for Diagnosis. ? Dermatomyositis.**—Dr. H. BLACK, for Dr. G. B. MITCHELL-HEGGS.

Granulomatosis Disciformis Progressiva et Chronica (Miesher).—Dr. P. HALL-SMITH, for Dr. G. B. MITCHELL-HEGGS.

OBITUARY.

DR. J. FREDERICK BURGESS, O.B.E., F.R.C.P.(C.).

CANADIAN dermatology and the international dermatological world sustained a great loss in the unexpected death in Montreal of Dr. John Frederick Burgess on 7 April 1953.

Although multiple episodes of ill-health had troubled him during the last decade, he surmounted these hazards and was active in practice until his untimely end. This was typical of the quiet courage of the man who faced the unknown future of dermatology at the finish of his Great War service, with but one arm to aid him in the major change from a surgical career to that of a new specialty. For distinguished service in France, Major Burgess received the Order of the British Empire from the hands of His Royal Highness the Prince of Wales at the time of his first visit to the Dominion.

Dr. Burgess pioneered in Montreal the newer concepts of investigative dermatology and the modern techniques of therapy. As the dermatologist to the Montreal General Hospital he built, upon the solid foundations laid by the late Francis Sheppard and Gordon Campbell, an expanding outdoor department, and he established a ward for the care of skin diseases. Appointed in 1931 the Clinical Professor of Dermatology, he brought to McGill a wealth of dermatological knowledge gained first from his alma mater, Toronto, and later added to from the post-graduate schools of Vienna, Paris and London.

Newer problems ever presented a challenge to his inquiring mind and in his search for their solution he stimulated his students and colleagues to follow with him along investigative trails. Undergraduate and post-graduate instruction were both major interests to him, and he was instrumental in creating a post-graduate Diploma Course in McGill University. His industry aided in the formation of the Section of Dermatology of the Royal College of Physicians and Surgeons of Canada, with its Certification and Fellowship awards.

The Montreal Dermatological Society and the Canadian Dermatological Association owe much to his memory. In these groups he was a charter member. He had served as Vice-President of the American Dermatological Association, as Director of the American Academy of Dermatology and as President of the Canadian Branch of the British Dermatological Association during its formative years. The Swedish Dermatological Society honoured him with a corresponding membership, as did the Dermatological Section of the Royal Society of Medicine in London. He was enrolled in the New York Academy of Sciences.

Dr. Burgess enjoyed the outdoor life, was a keen fisherman and a vigorous opponent at golf and tennis. Thanks to early studies in clinical mycology, he later became interested in classifying the fungi found in nature. Here his exact knowledge, reinforced by his fine colour transparencies of the mushroom family, soon raised him to a position of authority in this field. The rare and common dermatoses recorded on Kodachrome testify also to his gifts as a photographer. His modest and retiring demeanour did not deny to him a host of friends, and he particularly endeared himself to little children. All of these now feel the gap in their lives caused by his sudden passing.

L. P. E.

THE BRITISH ASSOCIATION OF DERMATOLOGY.

THE Thirty-third Annual Meeting of the Association was held in London on 25, 26 and 27 June 1953 under the presidency of Dr. J. E. M. Wigley. Eighty-seven members and thirty-one visitors attended the meeting.

The proceedings started with the Annual Business Meeting, at which it was resolved that foreign corresponding members should henceforth be given the title of Honorary Foreign Members. A form of certificate for presentation to honorary foreign members was approved.

The Secretary then conveyed to members an invitation from the Canadian Dermatological Association to meet with them in Toronto in 1955.

After the Editor's and Treasurer's reports had been received and approved the following officers were elected for the ensuing year:—

President : Dr. C. H. Whittle.

Treasurer : Sir Archibald Gray.

Hon. Secretary : Dr. G. B. Dowling.

Editor : Dr. F. Ray Bettley.

Assistant Editor : Dr. G. W. Bamber.

Ordinary Members of the Executive Committee : Dr. Robert Aitken (Edinburgh), Dr. Alice Carleton (Oxford), Dr. L. Forman (London), Dr. G. A. Hodgson (Cardiff), Dr. Brian Russell (London), Dr. J. Sommerville (Glasgow) Dr. H. J. Wallace (London), Dr. J. E. M. Wigley (London), Dr. D. I. Williams (London).

It was agreed that the thirty-fourth Annual Meeting be held in Cambridge in 1954.

The following were elected Honorary Members : Dr. Rupert Hallam, Dr. Louis Savatard, Sir Norman Paul.

The following were elected Honorary Foreign Members : Professor N. Danbolt (Norway), Professor F. Flarer (Italy), Professor M. I. Quiroga (Argentina), Dr. A. Touraine (France).

The following Ordinary Members were elected : Dr. Geoffrey Auckland, Dr. Patrick Hall-Smith, Dr. J. S. Pegum, Dr. Bethel Solomons, Dr. W. Tillman.

The Meeting recalled in sorrow the death of Dr. Harold Orr, Dr. F. S. Cliff and Dr. J. F. Burgess.

The Scientific Meeting began with a discussion on "Peripheral Vascular Disorders of the Skin" (Professor A. M. Boyd, Dr. D. S. Wilkinson, Dr. Ian H. Whimster). This discussion occupied the rest of the morning and was followed in the afternoon by the following short papers : "The Fate of Melanocytes within the Epidermis" (Dr. R. E. Billingham), "Contribution to the Pathogenesis of Scleroderma" (Dr. L. A. M. B. Musso, Dr. R. H. Seville, Dr.

R. Reed), "The Value of Antihistamines in the Treatment of Urticaria" (Dr. R. Warin).

The next day was devoted to a discussion on "Rosacea, with Special Reference to its Ocular Manifestations" (Mr. A. J. B. Goldsmith, Dr. Peter Borrie). An interesting discussion followed these papers and the morning came to an end with two short papers: "Acneiform Eruptions in Children" (Dr. F. F. Hellier), "The Skin in General Literature" (Dr. W. R. Bett). There was no meeting in the afternoon.

More short papers occupied the whole of Saturday morning: "Ocular Pemphigus" (Dr. I. B. Sneddon and Dr. R. E. Church), "Bullous Pemphigoid Eruption" (Dr. A. F. Rook and Dr. E. R. Waddington), "Bullous Pemphigoid Eruption in Children" (Dr. G. B. Dowling and Dr. R. H. Meara), "The Effects of Measured Friction on the Skin" (Dr. P. Naylor), "Proteinase Activity of Skin" (Dr. Ian Magnus).

On Saturday afternoon a Clinical Meeting was held in the Out-patient Department of St. Thomas's Hospital. Thirty-six cases were shown and briefly discussed afterwards.

The reception and annual dinner was held in the Grocers' Hall, Princes Street. This magnificent building, finely appointed, contributed much to the success of the evening. The principal speakers were the President, Dr. J. E. M. Wigley, Sir Francis Walshe, Dr. H. R. Vickers and Dr. Geoffrey Hodgson. After dinner Dr. Grant Peterkin was presented with the B.A.D.S. Golf Challenge Cup which he had won that afternoon.

On Thursday evening we were invited to the Presidential reception, where Dr. and Mrs. Wigley entertained us on a river launch. This original form of reception was not without its risks, for the weather during the first three weeks of June had been exceptionally cold and wet. As it happened, the President was fully justified, for the evening was the warmest and most agreeable we had so far experienced this year. In the warm sun with a cooling breeze we left Westminster Pier and went as far as Battersea Gardens; here we turned and followed the River down to beyond Greenwich. And so we returned as dusk came on and the Coronation floodlights lit up Tower Bridge and the Embankment.

In years to come we are likely to look back on our thirty-third meeting and to value it as one of the most successful we have ever had.

BOOK REVIEWS.

PRACTICAL DERMATOLOGY.*

THIS is not intended to be a reference book, but is a practical guide for students and general practitioners. It fulfils this purpose admirably.

The basic related fields of histology, mycology, etc., have been omitted. The subject matter is clearly written and easily understood. The opening chapter on diagnostic methods is excellently presented and should prove very helpful for students and practitioners. The chapter on skin and other organs stresses their inter-relationship and briefly recapitulates the more important associations. An up-to-date indexed, numbered, pharmaceutical formulary is included.

The monochrome illustrations are small, but on the whole very good. The book is carefully indexed, printed on excellent paper, and beautifully bound. J. S.

ATLAS OF SKIN AND VENEREAL DISEASES.†

PROFESSORS ARZT and Tappeiner have now completed a magnificent atlas of skin and venereal diseases which adds lustre to the work of the Vienna School. The work is dedicated to the memory of the famous founder of this School, Ferdinand von Hebra, to commemorate the 100th anniversary of his appointment as extraordinary Professor. His portrait forms a very appropriate frontispiece to the first volume.

All the illustrations are reproductions of water colour drawings prepared under the direction of an artist, Professor Dietz, who has been amazingly successful in producing lifelike pictures of such a variety of skin conditions.

Volume I shows, in 266 pictures, a great variety of the lesions of syphilis and thereby covers all the commoner manifestations and many of the rarer. In these days when syphilitic lesions are becoming much less frequent, it becomes all the more necessary to have reliable pictorial records of them, so that the student does not forget the existence of this disease when suddenly confronted with an isolated case.

Volume II has 411 pictures of skin conditions other than syphilis. The authors have been most careful to choose typical examples of all the commoner skin diseases and have not been beguiled into illustrating a large number of rare conditions, though a few of the more important of these have been included.

The atlas is one which teachers will find most valuable in instructing students and they will also find in it much to interest the advanced worker. The authors and publishers are to be congratulated on having produced a very fine and useful publication. A. M. H. G.

PIGMENTATION AND FUNCTION OF THE SUPRARENAL CORTEX IN BLACK AND WHITE SKINNED RACES.‡

THE author believes that the comparative study of different races may shed a light on physiological processes and also on the mechanism of evolution. He analyses

* *Practical Dermatology*. GEORGE M. LEWIS, M.D., F.A.C.P. (New York). W. B. Saunders & Co., 1952. Pp. 358 (incl. Index). Plates 99. Price 37s. 6d.

† *Atlas der Haut und Geschlechtskrankheiten*. LEOPOLD ARZT and JOSEF TAPPEINER. Vienna: Urban and Schwarzenberg. Vol. I: "Geschlechtskrankheiten" 1950. Swiss francs 90. Vol. II: "Hautkrankheiten" 1953. Swiss francs 170.

‡ *Pigmentation and Function of the Suprarenal Cortex in Black and White Skinned Races*. JEANNE LESCHI. Masson & Cie., Editeurs, Libraires de L'Academie de Medicine, 1952. Pp. 109. 13 Illus. Price 950 frs.

a lot of statistics, only some of which are his own personal observations, and reaches the conclusion that dark-skinned races show "hypoadrenalism" compared with white-skinned. This is based on the relative size and volume of the suprarenals, on estimations of the minerals in the serum, on the experimental production of hypokalaemia, etc. He feels that from his observations the role of the suprarenals in melanogenesis in man is more clearly defined.

F. F. H.

CORTISONE AND ACTH IN CLINICAL PRACTICE.*

Cortisone and ACTH have been used long enough for an interim appraisal of their use to be of value, and Dr. Copeman and his colleagues have timed this book cleverly so that it can be a help to those who wish to use the long promised increased supplies of these hormones.

In the first chapter Dr. Copeman reviews the chemistry of ACTH, cortisone and hydrocortisone and alterations in body metabolism resulting from their use. He then deals with their effects on specific tissues and on alterations of the sedimentation rate and blood pressure. Then follows a lucid account of the use of the hormones in rheumatic diseases which is based both on published work and on the author's own experiences. The possible toxic effects of ACTH and cortisone are discussed in detail, and the importance of thorough investigation of the patient and careful selection of cases before treatment as a means of avoiding side-effects is stressed.

A complete chapter on the treatment of skin diseases is contributed by Dr. Mitchell-Heggs. Although he repeats perhaps unnecessarily much of the account of the physiology and side-effects of the hormones, this minor criticism is soon forgotten when reading his account of their use in treatment. He adopts a cautious and critical attitude when evaluating the effects of ACTH and cortisone on disseminated lupus erythematosus, the pemphigus group and dermatomyositis, and gives an admirable scheme of investigation and precautionary measures to be taken both before and during treatment of a case.

He is more optimistic about the results of treatment in exfoliative dermatitis and scleroderma. Clear indications for the use of ACTH and cortisone are the suppression of severe symptoms in self-limiting conditions such as acute contact dermatitis and drug eruptions, and desensitization under an umbrella of cortisone is described as a possibility. Other skin conditions considered are lichen planus, psoriasis, atopic eczema and sarcoidosis. The book is completed by chapters on diseases of the endocrines, the eye, the blood and the respiratory system.

The references are collected conveniently at the end of each chapter and the book is pleasingly produced. It is above all a readable and practical book and should find a place on every dermatologist's bookshelf.

I. B. S.

DERMATOLOGY: ESSENTIALS OF DIAGNOSIS AND TREATMENT.†

PERHAPS because Year Book publications, especially those relating to dermatology, have set such a high standard in the past, your reviewer found this book disappointing. The defects of the book are rendered more noticeable by the wealth of useful information contained therein.

It purports to provide the essentials of dermatological diagnosis and treatment for the general practitioner. In spite of a preface to this effect the authors do not

* *Cortisone and ACTH in Clinical Practice.* By W. S. C. COPEMAN. London: Butterworth & Co. Pp. 255. 29 figs. Price 25s. net.

† *Dermatology: Essentials of Diagnosis and Treatment.* By MARION B. SULZBERGER and JACK WOLF. Chicago: Year Book Publishers, Inc. Pp. 592. Illus. 508. Price \$10 (78s.). (Distributed in this country by Interscience Publishers Ltd.)

appear to have differentiated clearly between essential principles and the detailed information appropriate to a reference book. Thus the chapter on pruritus might well daunt all but the most obsessional practitioner, giving an inadequate idea of the incidence of the different causes of pruritus or of the value of various forms of treatment. Many might consider that for this disorder spinal puncture and epidural injections of saline were a little *recherche* for the general practitioner, apart from being of dubious value.

This confusing plethora of detail occurs in many of the sections on treatment, which often give the impression of a cross between an alchemist's dream and Mrs. Beeton in one of her more expansive moments. That this is all too common a failing in comparable books on dermatology does not lessen the irritation engendered by it, and possibly by some of the prescriptions suggested. Thus eighteen different prescriptions are given for the treatment of eczematous dermatitis, which are increased to twenty-one when considering atopic eczema. Fourteen prescriptions are given for fungus infections and seven for treatment of a scurfy scalp. In many sections on treatment the reader is left in doubt as to the true value of remedies that have been used for fifty years and more; surely by now a fairly accurate estimate should be possible and, if not, the practitioner should not be invited to join the confusion.

A less important criticism is the placing of a detailed section on treatment at the beginning of a book of this kind. This is now fairly standard practice, and is particularly understandable in this volume which derives from "Dermatologic Therapy". With this arrangement, however, your reviewer was almost constrained to read the book in Chinese fashion lest he be overwhelmed by a multiplicity of recipes.

In a subsequent edition mention might be made of the evil effects on the thyroid of the absorption of resorcin when allowed to come into contact with abraded skin over a long period.

There are many excellent chapters, the sections on allergic skin diseases being especially good. The illustrations vary greatly in quality and usefulness, the coloured illustrations being particularly fine. The book is beautifully produced and printed on excellent paper.

H. G. W.

CURRENT LITERATURE.

ULCUS TEREBRANS TREATED WITH RADIO-ACTIVE COBALT. F. AICHINGER. (1953) *Derm. Wschr.*, 127, 49.

An extensive ulcer terebrans affecting the middle part of the face including the nose was treated with a radio-active cobalt plastic mould 4-10 mm. thick. An exact impression was first obtained with a gelatine mould (glycerine 500 c.mm., gelatine 500 g., 500 c.c. water). The underlying bony structures were preserved as with Chaoul therapy. The smallest possible effective dosage was given. The average radiation of the mould was 105 r/h, but towards the eye where the mould was thinner 75 r/h. A Cadmium-Sulfid-Kristalldosimeter (Siemens) was used in determining the dosage of the plastic cobalt preparation (plastobalt). The dosage given varied according to the site, but the total dose for the nasal hollow was 987 r; 6 weeks after the first treatment biopsies still showed evidence of carcinoma in the depth of the right upper jaw but all other areas seemed clear. A small plastobalt mould 75 r/h to the still active area was applied for 18 hours, and still a third (1000 r) to very small area at the upper pole of the area found to be not yet quite clear 5 weeks later. No evidence of activity when last seen 6 months later. Total dose to border of ulcer 1560 r; centre of right upper jaw $2600 + 1260 = 3860$ r; to a central area of the ulcer hollow $3860 + 1000 = 4860$ r.

M. S. S.

APPLICATIONS SUITABLE FOR THE SKIN IN EXTERNAL DERMATOTHERAPY. K. HALTER and W. FALK. (1952) *Derm. Wschr.*, 126, 1121.

The authors compared the effect of treatment on two sides of the body in 125 patients with subacute and chronic eczema, acute and subacute dermatitis, endogenous eczema, seborrhoeic eczematide and sebastatic eczematide, and drug exanthem. They divided them into three groups according to the activity of the skin glands (greasy, 34; normal, 33; or dry skin with tendency to scale, 58. The largest group contained many elderly people, possibly some seborrhoeics in the sebastatic phase). The local applications consisted of lotio zinci and esiderm (fat-free); desitin, past. zinc. moll., zincol, and eucerine with lanoline, equal parts.

In seborrhoeic affections fat-free applications seemed most effective and best tolerated (28 of 34 patients); 6 yielded best to a grease-containing paste, while salves or purely fatty applications completely failed. In the group of intermediate secretion type (normal) a paste was most effective (27 of 33 patients); only 6 responded best to a purely fatty or fat-free application. The sebastatics with dry skin were found to the surprise of the authors to respond better to a grease containing paste than to a salve.

M. S. S.

THE TREATMENT OF SKIN TUBERCULOSIS WITH ISONICOTINIC ACID HYDRAZIDE (NEOTEBEN). R. BRETT and O. BRAUN-FALCO. (1953) *Derm. Wschr.*, 127, 1.

There were 51 patients (47 lupus, 1 Bazin's disease and 3 scrofuloderma). The dose was 4-6 mg. per kg. of body weight, i.e., from 0.3-0.4 g. daily, given 2-4 times daily. Appetite and weight increased in most patients and the response of the lesions to the treatment was rapid and very good. Nervous system side-effects were not encountered, but an occasional complaint was nausea (1), palpitation and excitement (1), dyspepsia due to hyperacidity (2) and giddiness in one or two. After a dose of about 40 g. no disturbance of the serum calcium, Takata or Weltmann reaction or of the serum bilirubin was noted. The E.S.R. improved, and occasionally the value at 1 hour was less than that at 2 hours. An increase of leucocytes was likelier than a diminution and an increase in segmented nuclei at the expense of lymphocytes. Specially noticeable was the fall in the Volhard water and concentration test. Diuresis was noted soon after the onset of treatment with a reduction in concentration. No abnormality was found in the urine. The severest forms of lupus of the face responded well, and in one patient uninfluenced by vigantol or conteben in massive doses. In most patients after 2-3 weeks succulence of the lesions disappeared, the patches became more and more a brown reddish shade, and apple jelly nodules became difficult to find. In no case did the drug lead to a local reaction as occasionally happens with vigantol. The conditions other than lupus vulgaris also responded well.

M. S. S.

EXPERIENCES UP TO DATE WITH NEOTEBEN (ISONICOTINIC ACID HYDRAZIDE) IN SKIN TUBERCULOSIS. O. GRÜTZ. (1953) *Derm. Wschr.*, **127**, 169.

All forms of skin tuberculosis (including Bazin's disease and papulo-necrotic tuberculide) responded well to 5-10 mg. per kg. of body-weight; mucous membrane lesions also. The longest period of treatment, 6 months. Side-effects were encountered in only 2 out of 34. Paraesthesia of the fingers in one subsided on stopping treatment; a petechial eruption of the legs in a second suffering from pulmonary tuberculosis subsided on stopping treatment, to recur on its resumption. M. S. S.

ULCERATED HYPERERGIC TUBERCULIDES (TUBERCULOSIS ULCEROSA CUTIS HYPER-ERGICA (v. d. Meer)). W. BRAUN. (1953) *Derm. Wschr.*, **127**, 148.

This is the likely diagnosis in this patient aged 64 with multiple ulcerated lesions (the largest of palm size) of lower limbs, arm and buttock and bone tuberculosis; previous mastectomy for tuberculous nodule. An intracutaneous tuberculin test with 0.1 cm. 1:1 mill. A. T. Koch led to a slowly healing ulcerated reaction. At first the intracutaneous A.T. reaction was negative, using a dilution of 10^{-16} . Tubercle bacilli could not be demonstrated directly or by animal experiment, but clinically and histologically the lesions were tuberculous. M. S. S.

BULLOUS ERUPTION OF THE SKIN IN A PATIENT FOLLOWING CARBON MONOXIDE POISONING. G. WEBER. (1953) *Derm. Wschr.*, **127**, 175.

Admitted severely ill after attempted suicide with gas, the patient developed bullae on the backs of the fingers of both hands 24 hours later; these became haemorrhagic, but healed without necrosis. Similar instances are cited. Treatment on admission consisted of hourly intravenous coramine and lobeline-sympatol with oxygen administration. M. S. S.

ISOPHASIC REACTION FOLLOWING EXPERIMENTAL SUPERINFECTION OF LEISHMANIA.

TROPICA. A. DOSTROVSKY, F. SAGHER and A. ZUCKERMAN. (1952) *Arch. Derm. Syph., Chicago*, **66**, 665.

Although a positive reaction to leishmanin (analogous to tuberculin) occurs early in leishmaniasis the development of immunity to superinfection is delayed until parasites are no longer found in the primary lesion. Though this immunity is usually permanent, relapsing cutaneous lesions may occasionally be found, and these differ from the primary lesions in having a tubercloid structure. Intradermal inoculation of one or 10 million organisms were made in 6 patients with such recurrent lesions, and in 5 lesions were produced having the same characters as the recurrent lesions. J. K.

CANDIDA ALBICANS: RAPID IDENTIFICATION IN PURE CULTURES WITH CARBON DIOXIDE ON MODIFIED EOSIN-METHYLENE BLUE MEDIUM. JULIA T. WELD. (1952) *Arch. Derm. Syph., Chicago*, **66**, 691.

This paper deals with pure cultures only, but we are promised in a subsequent one to be shown how the method can be successfully applied to clinical specimens. J. K.

FURTHER AMPLIFICATIONS OF THE CONCEPT OF DERMATOPHYTID. I. ERYTHEMA ANNULARE CENTRIFUGUM AS A DERMATOPHYTID. OTIS FIELD JILLSON and ROBERT A. HOEKELMAN. (1952) *Arch. Derm. Syph., Chicago*, **66**, 738.

The authors agree with the view that in some cases erythema annulare centrifugum is a dermatophytid, and cite 5 patients to prove it. In 2 of them they produced the condition by experimentally producing athlete's foot and abolished it by eradicating the infection. J. K.

RELATION OF GROWTH OF HAIR ON DIGITS TO THE SEVERITY OF ISCHAEMIA. M. NAIDA. (1953) *New Engl. J. Med.*, **248**, 179.

The hair growth on the toes of patients suffering from occlusive diseases of the popliteal or femoral arteries was studied in 173 patients.

It was found that ischaemic lesions of the toes nearly always healed if there was a good growth of hair, whereas if there was little or none amputation was generally required.

Observation of the hair growth, therefore, indicates whether or no spontaneous healing of a gangrenous lesion may be expected. A. D. P.

TREATMENT OF TUBERCULOSIS OF THE SKIN BY THE METHOD OF FANIELLE-CHARPY ALONE OR IN CONJUNCTION. M. CRAFS, S. LAPIERE and H. VAN RUNCKELEN. (1952) *Arch. belg. Derm. Syph.*, 8, 371.

The authors conclude that while the results obtained with massive doses of calciferol are better than those with actinotherapy a combination of the two is better still, and a preliminary course of dihydrostreptomycin and P.A.S. makes the treatment still more efficient. J. K.

DERMATITIS DUE TO ANTIHISTAMINE OINTMENTS. E. SIDI, G. R. MELKI and R. LONGUEVILLE. (1953) *Acta Allergol.*, 5, 292.

Of 331 cases of contact dermatitis, 37 resulted from sensitivity to histamine antagonists. Of these cases 20% became photosensitive, and many reacting to phenergan gave cross-reactions to other members of the "para" group. H. T. H. W.

UNUSUAL REACTION FOLLOWING USE OF PHENYLBUTAZONE (BUTAZOLIDIN). R. CHARET and I. SIEGEL. (1953) *J. Amer. med. Ass.*, 151, 556.

Butazolidin is chemically related to amidopyrine. Undesirable side-effects occur in 25% to 33% of cases. A case is reported of a severe febrile reaction with a generalized maculo-vesicular eruption and vesicles and ulceration of the lips, tongue and oral mucous membrane. A. J. R.

PUBLIC HEALTH CONVENTION. C. DUCREY, G. GALETTI and F. FRANCHI. (1952) *Dermatologia*, 3, 161-207.

This number is devoted to communications and articles arising out of the fourth convention of public health officers concerned with dermatitis and syphilis. Professor Ducrey outlines work done by this association in the growing recognition of the importance of preventive and occupational medicine in these spheres. The impression given is that Italians are very conscious of this importance and, although perhaps less experienced than Anglo-Saxon countries with their long and continuous tradition of national insurance, they are able to appreciate some of the shortcomings inherent in these systems and are trying to avoid them. Their outlook is, perhaps, more international than ours, and their work is closely integrated with that of other European countries.

The difficulty of defining occupational skin disease is underlined by an interesting table of comparative definitions in use in different countries, definitions which range from the widest possible to attempts at exact limits. An interesting one comes from Czechoslovakia—"chronic affections of the skin due to noxious substances that oblige the worker to change his occupation or to abandon remunerative employment." It is applicable to all enterprises in which the insured person is exposed to risk. D. S. W.

BONNEVIE-ULLRICH SYNDROME. B. CARLETTI and L. PARENZAN. (1952) *Giorn. ital. Derm. Sif.*, 93, 48.

A clear and useful article by paediatricians on this curious syndrome of which one or two examples have been shown recently. Its importance to dermatologists lies in its presenting feature of swelling and tumefaction of the hands and feet soon after birth. The other characteristics are webbing of the neck, hypoplasia of the muscles and anomalies of their insertion, syndactyly, and various bony deformities, retardation of growth and sexual function, anomalies of the cranial nerves, laxity of the skin and malformations of the nails. The authors believe that this is the same condition as described by Turner, by which name an associated syndrome is more commonly known in England. They discuss theories of causation without very much enthusiasm for any one of them. D. S. W.

LIBMAN-SACHS SYNDROME. V. PASTORINO. (1952) *Giorn. ital. Derm. Sif.*, 92, 120.

A review of a case of Libman-Sachs disease and the consideration of its relationship with acute lupus erythematosus. The author feels that it is still justifiable to regard these two conditions as distinct. D. S. W.

STUDY OF THE URINARY PORPHYRINS: PORPHYRINS AND THEIR METABOLISM IN CONGENITAL PORPHYRIA.—(I.) F. OTTOLENGHI-LODIGIANI and G. SERCHI. (1952) *Giorn. ital. Derm. Sif.*, 92, 77.

The authors base their studies on a case of congenital porphyria with skin lesions, and in this communication make a detailed study of the urinary porphyrins. There is a very clear review

of the chemical structure of porphyrins and the methods of investigation of these by chromatography and extraction analysis. There are some interesting photographs of porphyrin crystals obtained by the latter method. This article forms a useful background to the present work being done on this subject with isotopes. D. S. W.

STUDY OF THE URINARY PORPHYRINS: PORPHYRINS AND THEIR METABOLISM IN CONGENITAL PORPHYRIA.—(II) F. OTTOLENGHI-LODIGIANI and G. SERCHI. (1952)

Giorn. ital. Derm. Sif., 93, 1.

The authors pursue their investigations into this condition. The patient they were studying had faecal porphyrins (uro-, copro- and protoporphyrin I and III, coproporphyrin predominating). The same porphyrins were present in a concentration of 25.2 mg. % in the duodenal juice. Coproporphyrin was also eliminated via the stomach and the salivary glands. Plasma and erythrocytes may show a completely different porphyrin content, coproporphyrin, for instance, being present in the latter but not in the former. In this patient the plasma concentration was 5000 times the physiological level. The isomer III predominated in all the material. The authors feel from the result of their investigations that it may be impossible to distinguish congenital and acute porphyria. Although they think the conditions are probably the same, they feel that the differences are sufficient for them to be kept separate clinically. Gray has already pointed out that in congenital porphyria (but not in acute) there may be a varying degree of haemolysis. It is difficult to read about the chemistry of porphyria for long without feeling that it resembles the interior of Ali Baba's cave—colourful, but with a strictly limited right of entry. D. S. W.

PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA (MUCHA'S DISEASE). P. CACCIALONZA and A. G. BELLONE. (1952) *Giorn. ital. Derm. Sif.*, 93, 257.

Habermann's name for this disorder, first described definitively by Mucha in 1916, has taken precedence over the 32 other names given at one time and another. A disease of young males rather than females, it has three forms, acute, acute becoming chronic, and chronic with acute flares; most cases last from five weeks to six months, but some much longer. Lymphatic enlargement is common; the aetiology is obscure (? virus, ? necrotic allergic disorder). Forms of passage indicate a relationship to the main group of guttate parapsoriasis. Though not uncommon in this country, the case presented is the first in the Italian literature. Virus studies were inconclusive; there was splenomegaly and eosinophilia. D. S. W.

HISTOCHEMICAL METHOD IN STUDY OF NORMAL AND ABNORMAL VASCULARITY OF THE SKIN. T. RIGGIO. (1952) *Giorn. ital. Derm. Sif.*, 93, 291.

A brief review of this staining method (benzedine and sodium nitroprusside) and its value in neurology and medico-legal problems. Applied to the study of the dermal capillaries, it shows an anatomical arrangement that corresponds with findings by other methods; in some pathological conditions studied the pattern was abnormal. A further study in purely vascular conditions might be warranted, but the method has limitations. See however the recent article by Leach in this Journal. D. S. W.

"INDUCTION" TROUBLES IN DERMATOLOGY. A. TOURAINE. (1951) *Minerva Medica*, 26, 53.

A further elaboration of the author's view on the theory of "induction"—failure leading to naevi and naevoid conditions. Originally put forward by Spemann, Mangold and others, it is admittedly pushed beyond its original concept by Touraine, who finds in it, however, a "satisfying pathogenic explanation" for the whole range of naevi, early, late, mixed, systematized and regional. Through the presence of certain cells (organizers) there exists a soluble chemical substance of the sterol group, containing a phenanthrene radical, which is the evoking agent. (These conductors are apparently non-specific, inheritance providing the individual characterization).

The author discusses the dermatological applications, clarifying naevi, naevoid conditions and dysplasias into groups due to hyper-, hypo- and dysinduction mechanisms; and into local, disseminated, regional and general types. Touraine admits the objections which exist to the theory. There is little evidence, for instance, for the presence of such special cells in the young embryo, but he feels able to meet these objections, and gives his reasons. A sheet-anchor for those who are at sea amongst naevi; an interesting conception to others, a worth-while article with the rest of the French references (which are scattered). D. S. W.

THE SKIN MANIFESTATIONS OF MALIGNANT DISEASE. L. FORMAN. (1952) *Brit. med. J.*, 2, 911.

The "cachectic" skin is observed particularly in relation to malignant disease of the gastrointestinal canal.

Pruritus is a frequent symptom of carcinomas, reticuloses and leukaemias.

Dilatation of the capillaries localized as spider naevi or angiomata or diffuse telangiectasia of the palms and soles has been observed with carcinoma.

Disease of the liver has been associated with telangiectasia of the face and palms.

Acanthosis nigricans, in which there is hypertrophy and pigmentation of the skin, in adults, is in most cases associated with malignancy.

The mechanism of some of these processes is discussed.

B. A. T.

MILIARY TUBERCULOSIS IN A CASE OF ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS TREATED WITH ACTH. BETTY WALKER. (1952) *Brit. med. J.*, 2, 1076.

Miliary tuberculosis occurred in a patient with acute disseminated lupus erythematosus being treated with ACTH. After two years there is no clinical or laboratory evidence of activity of the lupus. The tuberculosis was adequately controlled by streptomycin.

B. A. T.

EFFECT OF CORTISONE UPON SKIN SENSITIVITY TO TUBERCULIN IN SARCOIDOSIS. D. A. PYKE and J. G. SCADDING. (1952) *Brit. med. J.*, 2, 1126.

The effect of cortisone upon skin sensitivity to tuberculin was investigated in 14 patients with sarcoidosis. Ten patients who failed to react to at least 100 tuberculin units intradermally received 100 mg. of cortisone daily. In 8 of these a transient sensitivity to tuberculin was detected after intervals varying from 6-17 days.

Of nine patients similarly treated with cortisone, a reaction with induration and erythema persisting at least 48 hours was noted in 7 patients.

B. A. T.

TESTING OF SKIN DISINFECTANTS. PETER STORY. (1952) *Brit. med. J.*, 2, 1128.

Several disinfectants are compared by their ability to kill *Staph. pyogenes*, *Esch. coli*, *Ps. pyocyanea* and *Proteus vulgaris* on the skin.

1% iodine or 1% cetrimide in 70% industrial spirit killed all test organisms within 30 seconds, and 70% spirit alone produced "virtual disinfection" within that time. 10% cetrimide or 1/1000 dynium chloride in 70% spirit and 1% aqueous iodine were effective within 30 seconds against the bacteria tested.

B. A. T.

TREATMENT OF LUPUS VULGARIS WITH ISONIAZID. L. C. GOLDBERG and C. R. SIMON. (1953) *J. Amer. med. Ass.*, 151, 640.

Two patients with lupus vulgaris of over 30 years' duration were treated with Isoniazid (isonicotinic acid hydrazide). The response to treatment was dramatic and a section showed disappearance of the granulomatous infiltrate. A dose of 4 to 5 mg. per kilo of body-weight is well tolerated, and the authors suggest that a smaller dose should be continued for some time after clinical and histological cure as no information on the relapse rate is yet available.

A. J. R.

PENICILLIN ANAPHYLAXIS. P. S. MAYER, M. M. MOSKO, P. J. SCHUTZ, F. A. OSTERMAN, L. H. STEEN and L. A. BAKER. (1953) *J. Amer. med. Ass.*, 151, 351.

Of 6 patients with anaphylactic-like shock due to penicillin hypersensitivity all had had penicillin before, and 4 had had previous hypersensitivity reactions. The authors' experience and reports in the literature suggest that the immediate wheal reaction to intradermal testing may be useful in discovering those individuals susceptible to this severe type of reaction.

A. J. R.

SALICYLIC ACID POISONING IN DERMATOLOGICAL THERAPY. E. P. CAWLEY, N. T. PETERSON and C. E. WHEELER. (1953) *J. Amer. med. Ass.*, 151, 372.

Salicylic acid applied to large areas of skin may cause systemic poisoning. Two cases of poisoning from the use of salicylic acid in dermatological therapy are reported. Both patients were children (aged 10 and 6) and salicylic acid ointment (2% to 5%) had been applied to large areas of skin.

A. J. R.